UNIVERSIDADE FEDERAL DO PARANÁ

FLÁVIO AUGUSTO VIEIRA FREITAG

ASSOCIAÇÃO DO BLOQUEIO DO PLANO TRANSVERSO DO ABDÔMEN (TAP-BLOCK) COM O BLOQUEIO DO PLANO SERRÁTIL (SP-BLOCK) EM CADELAS SUBMETIDAS A MASTECTOMIA

CURITIBA

2019

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Dissertação apresentada ao curso de Pós-Graduação em Ciências Veterinárias, Setor de Ciências Agrárias, Universidade Federal do Paraná, como requisite parcial à obtenção do título de Mestre em Ciências Veterinárias.

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Orientador: Prof. Dr. Juan Carlos Duque Moreno

Coorientadora: Profa. Dra. Tilde Rodrigues Froes

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CURITIBA, 14 de Junho de 2019.

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EDUARDO RAPOSO MONTEIRO
Avaliador Externo (UFRGS)

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RESUMO

Objetivo Definir pontos de referência e a dispersão de diferentes volumes de injeção para o bloqueio do plano serrátil superficial (SSP block) em cadáveres de cães. Avaliar a analgesia intra e pós-operatória produzida com a associação do TAP block ao SSP block em cadelas submetidas a mastectomia total unilateral. **Design experimental** Estudos prospectivos, aleatórios, experimentais cadavérico e clínico. **Animais** Um cadáver de cão formalizado, quinze cadáveres de cães adultos descongelados e trinta e dois cães com neoplasias mamárias. **Métodos** A parede torácica do cadáver formalizado foi dissecada em um primeiro momento para identificação dos músculos da parede torácica e dos nervos encontrados no plano fascial entre os músculos músculo serrátil ventral torácico e grande dorsal. Em seguida, com um transdutor linear de ultrassom colocado sob a quarta e quinta costela, no nível da articulação do ombro, o bloqueio do SSP foi realizado nos dois hemitórax de 15 cadáveres de cães. Os 30 hemitórax foram distribuídos aleatóriamente para receber 0,3; 0,6; e 1 mL kg^{-1} de uma solução 1:1 de azul de metileno a 0,5% e ropivacaína a 0,375%. A solução foi depositada no plano fascial entre o músculo serrátil ventral torácico e grande dorsal e após 15 minutos os cadáveres foram dissecados para confirmar a correta localização e avaliar a dispersão da solução. Os cães com tumores mamários foram distribuídos em quatro grupos (n = 8) que receberam meloxicam (MxG), metadona (MtG), TAP block + SSP block (LG), ou todos os tratamentos combinados (TG). A resposta à estimulação nociceptiva foi avaliada durante a cirurgia e as pacientes foram avaliadas antes da pré-medicação e 1, 2, 3, 4, 6, 8, 12, 16, 20 e 24 horas após a extubação pela escala composta de Glasgow (CMPS-SF) e escala visual analógica. Dor foi considerada quando CMPS-SF $\geq$ 6 e metadona foi utilizada como resgate. **Resultados** A principal inervação no plano superficial serrátil são os ramos cutâneos laterais dos nervos intercostais. A taxa de sucesso do SSP block foi de 89.66% (26/29). Para os grupos 0,3; 0,6 e 1 mL kg^{-1} a dispersão do corante foi de 4,12 ± 1,12; 3,75 ± 0,93 e 5,00 ± 1,32 dermátomos, respectivamente. Não houve diferença significativa entre os grupos. No estudo clínico observou-se que todos os grupos necessitaram de resgate analgésico com fentanil durante a cirurgia. No período pós-operatório o número de animais resgatados nos grupos MxG, LG, TG e MtG foi de 0, 2, 1 e 3, respectivamente, sem diferenças entre grupos. Contudo, o número total de regates foi maior em MtG (15) do que em MxG (0), LG (3) e TG (1) (p = 0,002). **Conclusão** O SSP block pode ser facilmente realizado em cães e o volume de 0.3 mL kg^{-1} é suficiente para obter dispersão do anestésico local compatível com o bloqueio dos ramos cutâneos laterais de T1 a T9, conferindo analgesia da parede lateral do tórax em cães. A associação do SSP com o TAP block pode ser utilizada no contexto de analgesia multimodal, para proporcionar analgesia pós-operatória em cadelas submetidas à mastectomia total unilateral.

Palavras-chave: Analgesia; anestesia local; cães; cirurgia oncológica; tórax.

ABSTRACT

Objective Cadaveric study of landmarks and volume dispersion of superficial serratus plane block (SSP block) in dogs and clinical evaluation of nociceptive and pain stimulation in dogs submitted to mastectomy receiving the association of TAP and SSP block. **Study design** Prospective experimental randomized cadaveric and clinical study **Animals** One formaldehyde solution-preserved dog cadaver, fifteen frozen adult dog cadavers and thirty-two dogs with mammary tumors. **Methods** The formaldehyde cadaver thoracic wall was dissected in the first moment. After that with the ultrasound transducer placed over the fourth and fifth ribs, at the level of the shoulder joint, SSP block was performed 30 times, using different volumes (0.3, 0.6 and 1 mL kg^{-1}) of blue methylene solution, with a needle between the serratus ventralis thoracis and latissimus dorsi muscles. Cadavers were dissected to confirm and evaluate dispersion. Dogs with mammary tumors were divided in four groups (n = 8 each). Analgesia treatment was meloxicam (MxG), or methadone (MtG), or TAP + SSP block (LG), or all them combined (TG). Nociceptive stimulation was evaluated during surgery and patients were evaluated before premedication and at 1, 2, 3, 4, 6, 8, 12, 16, 20 and 24 hours after extubation, with CMPS-SF and VAS. Pain was considered when CMPF-SF scores ≥ 6 and methadone was used as rescue analgesia. **Results** The main innervation at the superficial serratus plane were the lateral cutaneous branches of intercostal nerves. SSP block success rate was 89.66% (26/29). For groups 0.3, 0.6 and 1 mL kg^{-1} dye dermatomal spread was of 4.12 ± 1.12, 3.75 ± 0.93 and 5.00 ± 1.32, respectively. No statistically significant difference was seen between groups. Clinical study results included that all groups needed analgesic rescue during surgery. At postoperative period the number of animals that receive rescue at MxG, LG, TG and MtG was of 0, 2, 1 and 3 respectively, without difference between the groups. However, the total number of rescues was higher at MtG (15) than in MxG (0), LG (3) and TG (1) ($p = 0.002$). **Conclusion** SSP block can be easily performed and a volume of 0.3 $mL.kg^{-1}$ may be sufficient for hemithorax analgesia in dogs. The association of SSP and TAP block may be used in the context of multimodal analgesic protocol, to provide postoperative analgesia in dogs submitted to total unilateral mastectomy.

Key-Words: Analgesia; dog; local anaesthesia; thorax; oncology.

SUMÁRIO

1. Introduction

Cancer prevalence in dogs and cats has increased considerably in the last years. The increase in the incidence of neoplastic diseases has several reasons, among them is the greater longevity observed in these animals, when compared to the past. Factors such as balanced nutrition, vaccines preventing the infectious diseases, precise diagnostic methods and also the increasingly specific and effective therapeutic protocols contribute to the greater longevity seen in dogs and cats (Withrow & Macewen, 1996; Maria et al. 1998; Morrison, 1998).

According to Maria et al. (1998) and Sanches et al. (2000), a high incidence of mammary tumors was detected followed by venereal transmissible tumors in dogs. Other neoplasms include skin tumors, soft tissue sarcomas, bone sarcoma, lymphoma and others. Mammary tumors represented approximately 50 to 70% of all tumors in female dogs, with 50% of these cases with some degree of malignancy (Gorman & Dobson, 1995; Withrow & Macewen, 1996; Moe, 2001; Merlo et al. 2008).

All tissue injuries, even secondary to elective procedures, can cause pain. This pain induces a stress response, mediated by the endocrine system, leading to an increase in the plasma concentrations of cortisol, catecholamine's and inflammatory mediators. Discomfort and unintentional pain associated with diagnostic, clinical and surgical procedures are easily neglected in veterinary patients, with oncologic pain being the major cause of negligence (Hellyer et al. 2007).

Total unilateral mastectomy is the most commonly used treatment for mammary tumors in bitches (Morris et al. 2011). Mastectomy requires the resection of the skin with a large margin of safety, in an attempt to avoid or minimize tumor recurrence or metastasis (Credie, 2013). The widespread dissection and removal of tissue at mastectomy is associated with severe pain in dogs and cats (Mathews, 2000). During the surgical procedure, the noxious stimulation is able to cause responses ranging from increased autonomic activity (increase of the heart rate, blood pressure, respiratory rate or all of them), important to be monitored during the trans operative period. The purpose of multi-modal anesthesia is to avoid central nervous system sensitization, reduce postoperative pain, improve the response to analgesics administered during recovery period and respect the ethical commitment to animal welfare (Fantoni, 2011).

The transversus abdominis plane block (TAP block) is a regional ultrasound-guided anesthesia technique, which aims to promote analgesia of the ventral and lateral abdominal wall, including the skin, mammary glands, subcutaneous tissue, musculature and parietal peritoneum (Schroeder et al. 2011; Castaneda-Herrera et al. 2017).

The serratus plane block (SP block) came with the objective of being an alternative to promote the hemithorax analgesia, with lower risks when compared to central neuraxial analgesia or paravertebral anesthesia (Blanco et al. 2013). It can be performed in the superficial (Superficial serratus plane block – SSP block) or in the deeper fascia of serratus ventralis thoracis. As TAP block, this is a technique of regional anesthesia and depends on the use of ultrasound, and is reported to promote breast analgesia in humans (Zocca et al. 2016).

Although it is a relatively well-known technique used by several professionals in the anesthesia clinical practice, the scientific literature of the clinical use of TAP block in dogs is limited (Schroeder et al. 2011; Bruggink et al. 2012; Portela et al. 2014; Castaneda-Herrera et al. 2017; Drozdzynska et al. 2017; Freitag et al. 2018). On the other hand, there is just one report regarding the use of SP block in dogs, but no anatomical evaluation was performed and the landmarks used in the study can be questioned (Teixeira et al. 2018). For these reasons, it is proposed to associate the two techniques with the aim of providing analgesia of the entire mammary chain and associated tissues, this reducing both the amount of general anesthetics required during surgery and the amount and dose of analgesic drugs used in the postoperative period, reducing the immunosuppressive potential associated with anesthesia and improving patient comfort.

2. General Objective

Evaluate the association of TAP block and SSP block for surgical anesthesia and control of postoperative pain in bitches undergoing total unilateral mastectomy.

2.1. Specific objectives

- Describe and standardize the superficial serratus plane block (SSP block) technique in dog cadavers;
- Determine the best volume for use in SSP block in dogs;
- Evaluate the analgesic effects of the association of TAP and SSP block in dogs undergoing to total unilateral mastectomy during the transoperative period;
- Evaluate the postoperative analgesia promoted by the association of TAP and SSP block in dogs undergoing to total unilateral mastectomy.

3. Dissertation format and consideration

The dissertation presented here, was formatted using the authors guide of the Veterinary Anesthesia and Analgesia (VAA) from Elsevier. The first chapter is already submitted to VAA, and currently waiting the second revision.

4. Chapter One

Ultrasound-guided superficial serratus plane block in dogs: an anatomical evaluation and volume dispersion study

Ultrasound-guided superficial serratus plane block in dogs: an anatomical evaluation and volume dispersion study

Authors

Flavio Augusto Vieira Freitag[a] (E-mail: flavio_freitag@hotmail.com)

Thalise da Silva Gaio[a]

Amanda Aparecida Mazur dos Santos[a]

Eloisa Muehlbauer[a]

Marcello Machado[b]

Juan Carlos Duque Moreno[a] (E-mail: anestesiologiavet@yahoo.com.br)

Authors Affiliation

A. Veterinary Sciences Graduate Program, Department of Veterinary Medicine, Federal University of Paraná. Postal Adress: Rua dos Funcionários 1540, Juvevê, Curitiba – PR, Brazil. CEP 80.035-050.
B. Anatomy Department, Biological Science Sector, Federal University of Paraná. Postal Adress: Avenida Coronel Francisco H dos Santos, Jardim das Americas, sem número, Curitiba – PR, Brazil. CEP 80.050-540.

Correspondence Author:

Juan Carlos Duque Moreno

Department of Veterinary Medicine, Federal University of Paraná. Rua dos Funcionários 1540, Juvevê, Curitiba – PR, Brazil. CEP 80.035-050, Brazil.

Phone number: 55 41 3350-5810

Cellphone: 55 41 9 9173-3606

E-mail: anestesiologiavet@yahoo.com.br

Authors' Contribuitions

FAVF: Study design, acquisition of data, analysis and interpretation of data, preparation of the manuscript.

TSG: Acquisition of data, analysis and interpretation of data.

AAMS: Acquisition of data, analysis and interpretation of data.

EM: Acquisition of data, analysis and interpretation of data.

MM: Acquisition of data, analysis and interpretation of data, critical review of the manuscript.
JCDM: Study design, acquisition of data, analysis and interpretation of data, preparation and critical review of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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4.1. Resumo

Objetivo Realizar uma avaliação anatômica do plano serrátil em cães para estabelecer os pontos de referência ideais para o bloqueio do plano serrátil superficial (SSP block) e avaliar a dispersão da solução de azul de metileno com três diferentes volumes de injeção

Design experimental Estudo prospectivo experimental cadavérico

Animais Um cadáver de cão preservado em solução de formaldeído e quinze cadáveres de cães adultos congelados

Métodos A parede torácica do cadáver formalizado foi dissecada. O bloqueio do plano serrátil superficial foi realizado 30 vezes, com o transdutor de ultrassom colocado sob a quarta e quinta costal, no nível da articulação do ombro. Uma agulha foi inserida *in-plane* em sentido caudocranial até que pudesse ser visualizada entra os músculos serrátil ventral torácico e grande dorsal. Os cadáveres receberam uma solução de azul de metileno 0.5%/ ropivacaína 0.375% em solução 1:1 em volumes de 0.3, 0.6 e 1 mL kg^{-1} e foram dissecados para determinar a dispersão do corante.

Resultados Os músculos identificados na parede torácica foram o cutâneo do tronco, grande dorsal, obliquo abdominal externo, serrátil ventral torácico, escaleno, serrátil dorsal cranial e intercostal externo. Os principais nervos identificados foram os ramos cutâneos laterais dos nervos intercostais, nervos intercostobraquiais e nervo torácico longo. A taxa de sucesso do bloqueio foi de 89.66%. Em três hemitórax, a dispersão do corante ocorreu no plano profundo do músculo serrátil ventral torácico. Para os grupos 0.3, 0.6 e 1 mL kg^{-1} a dispersão do corante se espalhou por uma média de 4.12 ± 1.12, 3.75 ± 0.93 e 5.00 ± 1.32 dermatomos respectivamente. Nenhuma diferença estaticamente significativa foi observada entre os grupos para a dispersão do corante.

Conclusão O bloqueio do plano serrátil superficial pode ser facilmente realizado com auxílio de ultrassonografia, com sucesso na visualização dos pontos de referência, e um volume de 0.3 mL kg^{-1} pode ser suficiente para analgesia do hemitórax em cães. Estudos clínicos em cães são necessários para fornecer uma melhor compreensão desta nova técnica.

Palavras-chave: Anestesia, analgesia, cão, anestesia local, tórax.

4.2. Abstract

Objective To make an anatomical evaluation of the serratus plane in dogs to establish the optimal landmarks for a superficial serratus plane block (SSP block) and evaluate methylene blue solution dispersion with three different volumes of injection

Study design Prospective experimental cadaveric study

Animals One formaldehyde solution-preserved dog cadaver and fifteen frozen adult dog cadavers

Methods The thoracic wall of the formaldehyde cadaver was dissected. A superficial serratus plane block was performed 30 times, with the ultrasound transducer placed over the fourth and fifth ribs, at the level of the shoulder joint. A needle was inserted in-plane in a caudocranial direction until it could be visualized between the serratus ventralis thoracis and latissimus dorsi muscles. Dog cadavers received a 0.5% blue methylene/0.375% ropivacaine 1:1 solution at 0.3, 0.6 and 1 mL kg^{-1} and were dissected to determine the spread of the dye.

Results The muscles identified at the thoracic wall were the cutaneous trunci, latissimus dorsi, external abdominal oblique, serratus ventralis thoracis, scalenus, serratus dorsalis cranialis and external intercostal. The main nerves identified at the superficial serratus plane were the lateral cutaneous branches of intercostal nerves, intercostobrachial nerves and long thoracic nerve. The success rate of the block was 89.66%. In three hemithorax the dispersion of dye occurred deep to the serratus ventralis thoracis muscle. For groups 0.3, 0.6 and 1 mL kg^{-1} dye dermatomal spread for a mean of 4.12 ± 1.12, 3.75 ± 0.93 and 5.00 ± 1.32, respectively. No statistically significant difference was seen between groups for dye dermatomal spread.

Conclusion Superficial serratus plane block can be easily performed under ultrasound guidance, with successful visualization of the anatomical landmarks, and a volume of 0.3 $mL.kg^{-1}$ may be sufficient for hemi thorax analgesia in dogs. Clinical studies in dogs are required to provide better understanding of this new technique

Key-Words: Anaesthesia, analgesia, dog, local anaesthesia, thorax.

4.3. Introduction

Treatment of thoracic wall pain in animals can be challenging, since thoracic surgery and thoracic injuries are associated with high levels of pain (Beswick et al. 2016). The canine thoracic wall is mainly innervated by the dorsal, lateral and ventral cutaneous branches of the spinal nerves (Bailey et al. 1984). The use of local anesthesia in dogs to provide analgesia in thoracic wall trauma, thoracotomy or surgeries involving the thoracic mammary gland chain, has been described in dogs including: intercostal nerve block, segmental thoracic epidural anesthesia and thoracic paravertebral block (Portela et al. 2014; Corona & Novello, 2018; Portela et al. 2018). However, in people these techniques are associated with complications such as pneumothorax, dural puncture, intrathecal injection, hypotension, bilateral blockade, intravascular injection, infection, hematoma, neural fascicle damage, intrapleural injection and block failure (Finucane, 2007).

The serratus plane block (SP Block) is an ultrasound-guided regional anesthetic technique, as a modification of pectoral nerve block 1 and 2, which aims to provide low risk analgesia to the hemithorax as compared to thoracic paravertebral or neuraxial blockade in humans (Blanco et al. 2013). In humans the SP Block is performed within the fascial plane underneath, or superficial to, the serratus anterior muscle (Blanco et al. 2013; Mayes et al. 2016) and has been used clinically for post mastectomy pain syndrome treatment, breast surgery, thoracotomy surgery, post-thoracotomy pain and in multiple rib fractures (Kunhabdulla et al. 2014; Maldabushi et al. 2015; Takimoto et al. 2016; Zocca et al. 2016; Cassi et al. 2017; Khalil et al. 2017). To the date, there is only one report about the use of the SP block in dogs in which a multiple injection technique at the deep serratus plane was associated with the TAP block for total unilateral mastectomy (Teixeira et al. 2018).

Anatomical evaluation of SP Block using methylene blue or latex spread in human cadavers, suggests that analgesia is mediated by the blockade of the lateral cutaneous branches of the intercostal nerves, rather than a direct blockade of the intercostal nerves (Mayes et al. 2016). The superficial approach at the 4^{th} rib for SP block in human cadavers showed a methylene blue spread from the lateral cutaneous branches of intercostal nerves T2 to T5, with some variable spread up to T6, the long thoracic nerve, and occasionally the thoracodorsal nerve (Varghese et al. 2016). The SP block is a straightforward block for anesthetists with experience in the TAP block to learn (Nair et al. 2015).

In contrast to reports from human literature, Teixeira et al. (2018) used a dorsoventral approach to inject 0.3 mL kg^{-1} of 0.25% bupivacaine in each one of two points, in the fourth and ninth intercostal spaces, between the serratus ventralis thoracis muscle and the intercostal muscles. The absence of anatomical studies, the small number of animals used (4) and the local chosen for the administration of the anesthetic (one of the injections was performed at the 9^{th} intercostal space, where the serratus ventralis thoracis no longer exists), are factors of bias and warrant complementary studies.

We hypothesized that the SSP block can be performed in dogs by an approach similar to that used in humans, effectively reaching the sensitive innervation of the hemithorax with a reduced volume of ropivacaine.

The objective of this study was to make an anatomical evaluation of the serratus plane, define the best landmarks for performing the technique and evaluate the dermatomal spread of three different volumes of injectate into this plane in dog cadavers.

4.4. Materials and Methods

Preliminary study

An adult, male, mixed breed, dog cadaver, from the Veterinary Anatomy Laboratory from the Federal University of Paraná, preserved in 4% formaldehyde solution was used. A veterinary anatomist determined anatomical landmarks that could be used to locate the serratus ventralis thoracis muscle using ultrasound, and confirmed the main nerve branches and muscles present in the thoracic wall.

Animals

This project was submitted to the local commission on ethics on the use of animals of the Federal University of Paraná (UFPR, Brazil), and approved by the number 015/2018, rectified 06/2019.

A total of 15 frozen dog cadavers were included, obtained from veterinary hospitals in Curitiba, with owner permission for the participation of the animal in the research. There were 9 females and 6 males, from a variety of breeds (1 beagle, 1 daschund, 2 lhasa apso, 2 poodles, 1 rottweiler and 8 mixed breed) with a mean weight of 12.0 ± 5.6 kg, and different causes of death unrelated to this study. All the dogs were fully developed and had no external signs of trauma. The cadavers were thawed slowly for 48 hours before the day of use.

Superficial serratus plane block (SSP block)

The cadavers were numbered from 1 to 15, and each thoracic wall was named as A (right) and B (left) for randomization into the groups that received the three different volumes of the solution using the site 'random.org'. Each thoracic wall was considered a separate entity, so there were a total of 30 blocks with ten blocks performed in each group, all the blocks were performed by the same veterinary anesthesiologist (FAVF).

Body conformation parameters were obtained, such as bodyweight in kilograms, total body surface in m^2, spinal length (from the occipital bone to the first caudal vertebra) and thoracic circumference in cm, to evaluate if the animals were evenly distributed between groups.

The cadavers were clipped on both sides of the thorax from the caudal angle of the scapula to the iliac crest, and from the dorsal to the ventral midlines. A linear ultrasound transducer with frequency 7.5 – 12 MHz (Esaote MyLab Vet Gold, L523), was positioned perpendicular to the ribs, over the fourth and fifth ribs, at the level of the shoulder joint. Cutaneous trunci, latissimus dorsi, serratus ventralis thoracis and external intercostal muscles were identified, along with the two ribs in the ultrasound image.

With the cadaver in left lateral recumbency, a 20G 3.5' Tuohy needle (BD Perisafe^{TM}) was introduced in an in-plane, caudocranial, approach until it reached the fascial plane between the serratus ventralis thoracis and latissimus dorsi muscles. The needle was connected to a fluid extender and a three way stop cock, filled with 0.9% NaCl. Initially 1 mL of saline solution was injected to ensure the needle was correctly positioned. Correct positioning was confirmed if an anechoic 'bubble' was seen between the latissimus dorsi and serratus ventralis thoracis muscles. After confirmation, a solution of 0.375% ropivacaine and 0.5% methylene blue (1:1) was injected into the SSP. The time for performing SSP block from completion of ultrasound examination until the end of solution injection was timed.

After injection the dog was rotated into right lateral recumbency, and the same procedure was performed on the contralateral side. The total volumes used were: 0.3, 0.6 and 1 mL kg^{-1} at each side, for G0.3, G0.6 and G1 respectively. After blocks had been performed on both sides the dog was positioned in dorsal recumbency until the time of dissection.

Serratus plane dissection

Thoracic wall dissection was performed 30 minutes after the completion of the blockades, starting with the right side. All the dissections were performed by the same veterinary anatomist (MM), to standardize results.

In left recumbency, a rectangular flap of skin extending from the thorax to the caudal region of the abdomen was created. A straight dorsoventral incision from the dorsal midline at a tangent to the caudal angle of the scapula was performed to the ventral midline over the sternum, cranial to the cranial thoracic pair of mammary glands. A second incision was made along the ventral midline from this thoracic level to the pubic region, circumventing the prepuce in males. The third and last incision was made from the ventral midline straight to the dorsal midline, at a tangent to the iliac crest. The skin was reflected dorsally and the cutaneous trunci muscle cranially after incision, followed by incision and reflection of latissimus dorsi muscle to visualize the serratus ventralis thoracis muscle that lies beneath it. For better visualization, fat tissue was removed during the dissection and any excess of methylene blue solution was gentle dried by swabbing.

The success of the technique was assessed by both accuracy of injection ie was a right fascial plane block achieved and for the distance of solution dispersion. The solution dispersion in SSP was measured in cm, from cranial to caudal (CC) and dorsal to ventral (DV) maximum limits, dermatomal spread (number of nerve roots or nerve region when the nerve root was not fully preserved, using the rib number as the reference) and nerve branches stained with the solution for specific nerves. Nerve branches that could be visualized were evaluated and only when nerves were stained greater than 6 mm it was considered to be a successfully blocked.

Statistical analysis

Normality of data was assessed by the Shapiro-Wilk test. To check differences between groups, One Way ANOVA followed by Tukey test for normally distributed data (bodyweight, total body surface, spinal length and thoracic circumference) were performed. Non-normally distributed data (CC and DV dispersion and dermatomes spread) were analyzed by Kruskal-Wallis test followed by Tukey test. Differences were considered significant when $p < 0.05$. All statistical tests were performed using Sigma Plot for Windows 12.0 (Systat, CA, USA).

4.5. Results

The evaluation of the thoracic wall was performed from the most superficial to the deepest external thoracic fascia, at the level of the external intercostal muscles.

The cutaneous trunci muscle lies in the superficial fascia of the trunk and is the most superficial muscle of the lateral part of the thoracic wall. The latissimus dorsi muscle lies under the cutaneous trunci, on the dorsal half of the lateral thoracic wall. The external abdominal oblique muscle covers the ventral half of the lateral thoracic wall and the lateral and ventral parts of the abdominal wall. After cutting and reflecting cutaneous trunci and latissimus dorsi muscles, the serratus ventralis thoracis muscle is visualized at the level of the shoulder joint, covering the cranial half of the lateral thoracic wall up to the 7th rib, with the long thoracic nerve crossing horizontally over its lateral surface (Fig. 1a). The cranial limits of the serratus ventralis thoracis are the 1st rib and the serratus ventralis cervicis muscle, ventrally it extends to the scalenus and external oblique abdominal muscles, and medially it is bounded by the external intercostal muscles. In a closer view, the long thoracic nerve, the lateral cutaneous branches of intercostal nerves T4 to T7 and intercostobrachial nerve III can be seen on the ventral edge of the serratus ventralis muscle (Fig. 1b).

Body conformation parameters measured in the animals from each group (G0.3, G0.6 and G1) in the second part of the study were respectively: bodyweight 12.45 ± 5.95 kg, 12.05 ± 4.99 kg and 10.97 ± 6.73 kg; total body surface 0. 53 ± 0.17 m^2, 0.53 ± 0.16 m^2 and 0.48 ± 0.20 m^2; spinal column length 57.70 ± 12.66 cm, 58.35 ± 10.30 cm and 56.62 ± 12.83 cm; and thoracic circumference 51.66 ± 10.52 cm, 51.52 ± 9.56 cm and 56.62 ± 12.82 cm. For any of these parameters there was no statistically significant difference between the groups.

Initially each group had 10 hemithorax, before the beginning of the dissection. One hemithorax was excluded from the study at the start of the dissection due to a severe hemorrhagic pre-mortem lesion in the right thoracic wall, so 29 blocks were evaluated.

The SSP Block was performed successfully by the trained veterinary anesthetist in 89.66% (26 out of 29) of cases (Fig. 2). In failed blocks, the solution spread deep beneath the serratus ventralis thoracis muscle. A total of 26 blocks were evaluated (G0.3 n = 8; G0.6 n = 9; G1 n = 9). The mean time for performing the SSP block was 68.62 ± 25.78 seconds, 72.44 ± 18.42 seconds and 69.67 ± 23.96 seconds for the groups G0.3, G0.6 and G1 respectively. There was no statistically significant difference between the groups.

Methylene blue solution dye spread for G0.3, G0.6 and G1 respectively was 8.00 ± 2.42 cm, 10.22 ± 3.24 cm and 11.98 ± 5.23 cm in the craniocaudal direction and 8.35 ± 3.06 cm, 9.07 ± 2.34 cm and 8.42 ± 2.06 cm in a dorsoventral direction. There was no statistically significant difference between the groups.

Mean dermatomal spread for the dye in groups G0.3, G0.6 and G1 respectively was 4.12 ± 1.12, 3.75 ± 0.93 and 5.00 ± 1.32. The ribs stained by each group following dermatomal spread can be seen in table 1. There was no statistically significant difference between the groups. An example of a successful SSP block is shown in figure 3.

The long thoracic nerve was visualized in all thoracic walls evaluated and the serratus ventralis thoracis muscle was seen. However, the lateral cutaneous branches of the intercostal nerves were visualized in only 3/26 (11.54%) thoracic walls. Intercostobrachial nerves II and III were seen in 9/26 (34.61%) thoracic walls. The long thoracic nerve was stained with methylene blue solution in 23/26 (88.47%) of the hemithorax and the intercostobrachial nerves in 8/26 (30.77%), corresponding to 8/9 (88.89%) of the visualized nerves.

4.6. Discussion

In the literature this is the first time the superficial serratus plane block technique in dogs is described, with different volumes dispersion evaluation. The superficial serratus plane block is a fascial plane block that is easy for anesthetists with experience in ultrasound-guided nerve blocks to perform (Nair et al. 2015). Clinical experience with the SSP block in dogs in the routine caseload of our Veterinary Teaching Hospital had previously shown a good analgesia of the ipsilateral hemithorax. This study was designed to confirm the appropriate plane and volume of local anesthetic for a successful block and the nerve branches involved in SSP in dogs. Based on our cadaveric findings, 0.3 mL kg^{-1} for each block appears sufficient to achieve SSP block.

In the formaldehyde preserved dog cadaver, lateral cutaneous branches and the long thoracic nerve were visualized in the serratus plane, suggesting that administration of local anesthetic solution in this plane may provide hemithorax wall analgesia via blockade of the lateral cutaneous branches similar to the results found in humans by Mayes et al. 2016. It’s expected the thoracic wall analgesia in dogs in secondary to the block of lateral cutaneous branches from T2 to T11 (Bailey et al. 1984). In addition, other anatomical features observed in the fixed cadaver, such as the arrangement of the muscle layers according to the fasciae of the trunk, the position and relations of each muscle being studied, and the distribution of the regional nerve branches corroborate information found in veterinary anatomical literature (Guetty, 1986; Evans & DeLahunta, 2013).

The 15 dog cadavers used, represented a broad selection of breed, weight, and sizes, however there was no statistical difference in the thoracic wall conformation parameters between the groups.

There is a learning curve for performing ultrasound-guided nerve blocks, which applies even to experienced veterinary anesthesiologists. The procedure does not always run smoothly. In this study there were three failed blocks due to dispersion of injection under the serratus ventralis thoracis muscle. However, it is likely that this placement of the anesthetic would also result in thoracic analgesia as already described (Blanco et al. 2013). Mistakes during injection in our study was due to the condition of the cadaver, the amount of fat tissue and defrosting artifacts in two cadavers, and ultrasound image mistake in the third one. No complications associated with the SP block were reported in medical literature, nevertheless intrathoracic puncture and pneumothorax can occur if the tip of the needle is not correctly visualized in ultrasound. Several mistakes may occur during ultrasound-guided blocks, including needle advancement without visualization at the ultrasound, difficulty in visualizing the structures involved and failure to recognize if the needle is at the desired end point (Sites et al. 2004).

The choice of the superficial plane rather than the deep plane block, was due the larger area covered and longer duration of effect reported in the study by Blanco et al. (2013), and the positions of the lateral cutaneous nerve branches seen in the formaldehyde preserved cadaver. However, the deep SP block is reported to provide good analgesic support in people as an alternative to the superficial technique. Clinical and anatomical studies comparing both techniques in dogs are recommended for better understanding.

The methylene blue solution used in this study provides a visual representation of the physical spread of the solution in cadavers. *In vivo* spread might be different, since the sensory block appears to be greater than the spread of dye would suggest based on human previous studies. When clinical and anatomical studies are compared, a median dispersion between T3 and T7 in superficial SP block in cadavers compares to T2 to T8/T9 for sensory block *in vivo* (Blanco et al. 2013; Biswas et al. 2018). This suggests that the physical dispersion in cadavers may not represent the true dispersion and the area of effective analgesia in clinical practice. The median cadaveric dispersion (> 50% of chance of staining) of the solution in all volumes is from T1 to T6, with the possibility to go up to T9 with this technique, more cranial to the results found in humans (starting at T3) (Biswas et al. 2018).

Selection of the minimum effective volume of local anesthetic agent is important. Local anesthetics can be toxic and theoretically a toxic dose may be achieved if a patient receives bilateral or more than one high volume local block. Samples of 0.3, 0.6 and 1.0 mL kg^{-1} were chosen to compare the use of lower or higher volumes. The dermatomal spread over which the dye spread was used to predict the anesthetic field, and there was no statistical difference between different volumes of injection. This suggests that even low volumes (of 0.3 mL kg^{-1}) could produce appropriate analgesia, with lower risk of toxicity. In the literature, for humans, the volume recommended for SP blocks varies between authors, but volumes of 20, 30, 40 mL $side^{-1}$ or 0.4 mL kg^{-1} are described (Blanco et al. 2013; Khalil et al. 2017; Biswas et al. 2018).

This study has some limitations. The use of uncontrolled cadavers, since the cause of death or the preservation of the cadaver could affect the dispersion of the solution, the use of dye mixed with local anesthetic (spread may be different due to differences in viscosity/density between solutions), cold temperature of the cadavers, defrosting artifacts and the absence of respiratory movements are some of these limitations. In addition, the use of animals of different breeds and sizes might have influenced the results due to variation in thoracic wall conformation, although this represent a better clinical practice. The choice of dorsal recumbency was based on the position of the majority of thoracic wall procedures performed in our veterinary hospital.

In conclusion, the SSP block is an easy technique to perform and can provide hemithorax analgesia. Injection is made between the 4^{th} and 5^{th} rib at the level of the shoulder joint, between the latissimus dorsi and serratus ventralis thoracis muscles. There is no significant difference in the dispersion of dye between the different volumes used in this study, and based on our results 0.3 $mL.kg^{-1}$ may be sufficient for hemithorax analgesia. Clinical studies in dogs are needed to understand the clinical utility of this new technique.

4.7. References

Allred C, Liu Y, Katrikh A et al. (2017) Cadaveric Study of Serratus Anterior Block. Annals of Emergency Medicine 70, 4S, S84.

Bailey CS, Kitchell RL, Haghighi SS et al. (1984) Cutaneous innervation of the thorax and abdomen of the dog. American Journal of Veterinary Research 45, 1689-1698.

Beswick A, Dewey C, Johnson R et al. (2016) Survey of Ontario veterinarians' knowledge and attitudes on pain in dogs and cats in 2012. Canadian Veterinary Journal 57, 1274-1280.

Blanco R, Parras T, McDonnell JG, Prats-Galino A (2013) Serratus plane block: a novel ultrasound-guided thoracic wall nerve block. Anaesthesia 68, 1107-1113.

Cassi LC, Biffoli F, Francesconi D et al. (2017) Anesthesia and analgesia in breast surgery: the benefits of peripheral nerve block. European Review for Medical and Pharmacological Sciences 21, 1341-1345.

Corona D, Novello L (2018) Segmental thoracic epidural anaesthesia in a dog undergoing intercostal thoracotomy and lung lobectomy. Veterinary Record Case Reports 6, 1-6.

Evans HE, Lahunta A. *Miller's anatomy of the dog*. 4. ed. St. Louis: Saunders-Elsevier, 2013.

Finucane BT. Complications of Regional Anesthesia. 2. Ed. Springer, 2007.

Getty, R. *Anatomia dos animais domésticos*. 5. ed. Rio de Janeiro: Guanabara Koogan, 1986.

Khalil AE, Abdallah NM, Bashandy GM, Kaddah TAH (2017) Ultrasound-Guided Serratus Anterior Plane Block Versus Thoracic Epidural Analgesia for Thoracotomy Pain. Journal of Cardiothoracic and Vascular Anesthesia 31, 152-158.

Kunhabdulla NP, Agarwal A, Gaur A et al. (2014) Serratus Anterior Plane Block for Multiple Rib Fractures. Pain Physician 17, E549-E557.

Madabushi R, Tewari S, Gautam SKS et al. (2015) Serratus Anterior Plane Block: A new Analgesic Technique for Post-Thoracotomy Pain. Pain Physician 18, E421-E424.

Mayes J, Davison E, Panahi P et al. (2016) An anatomical evaluation of the serratus plane block. Anaesthesia 71, 1064-1069.

Nair AS, Sahoo RK, Ganapathy M, Mudunuri R (2015) Ultrasound guided blocks for surgeries/procedures involving chest wall (Pecs 1, 2 and serratus plane block). Anaesth, Pain & Intensive Care 19, 3, 348-351.

Portela DA, Romano M, Briganti A (2014) Retrospective clinical evaluation of ultrasound guided transverse abdominis plane block in dogs undergoing mastectomy. Veterinary Anesthesia and Analgesia 41, 319-324.

Portela DA, Verdier N, Otero PE (2018) Regional anesthetic techniques for the thoracic limb and thorax in small animals: A review of the literature and technique description. The Veterinary Journal 241, 8-19.

Sites BD, Gallagher JD, Cravero J et al. (2004) The learning curve associated with a simulated ultrasound-guided interventional task by inexperience anesthesia residents. Regional anesthesia and pain medicine 29, 544-548.

Takimoto K, Nishijima K, Ono M (2016) Serratus Plane Block for Persistent Pain after Partial Mastectomy and Axillary Node Dissection. Pain Physician 19, E481-E486.

Teixeira LG, Pujol DM, Pazzim AF et al. (2018) Combination of Transversus abdomens plane block and Serratus plane block anesthesia in dogs submitted to mastectomy. Pesquisa Veterinária Brasileira 38, 2, 315-319.

Varghese L, Johnson M, Barbeau M et al. (2016) The Serratus Anterior Plane (SAP) Block: An anatomical investigation of the Regional Spread of Anesthetic Using Ultrasound-guided Injection. The FASEB Journal 30, 1 supplement, 560.1-560.1.

Zocca JA, Chen GH, Puttanniah VG et al. (2017) Ultrasound-Guided Serratus Plane Block for Treatment of Postmastectomy Pain Syndromes in Breast Cancer Patients: A Case Series. Pain Practice 17, 1, 141-146.

4.8. Figures and Tables

Figure 1 – Dissected dog cadaver fixed in 4% formaldehyde solution for the study of the anatomical relations of the serratus ventralis thoracis muscle and the main nerve branches of the thoracic wall. a) Superficial muscles of the thoracic wall. b) Muscles of the middle and deep fascial layers of the thoracic wall and nerve branches on the lateral wall of the thorax. Legend: CT, cutaneous trunci muscle (cut); LD, latissimus dorsi muscle (incised in a and reflected in b); EOA, external oblique abdominal muscle; EI, external intercostal muscle; Ibn, intercostobrachial nerve III; LTn, long thoracic nerve; S, scalenus muscle; SVt, serratus ventralis thoracis muscle; Arrows, lateral cutaneous branches of the intercostal nerves IV, V, VI and VII.

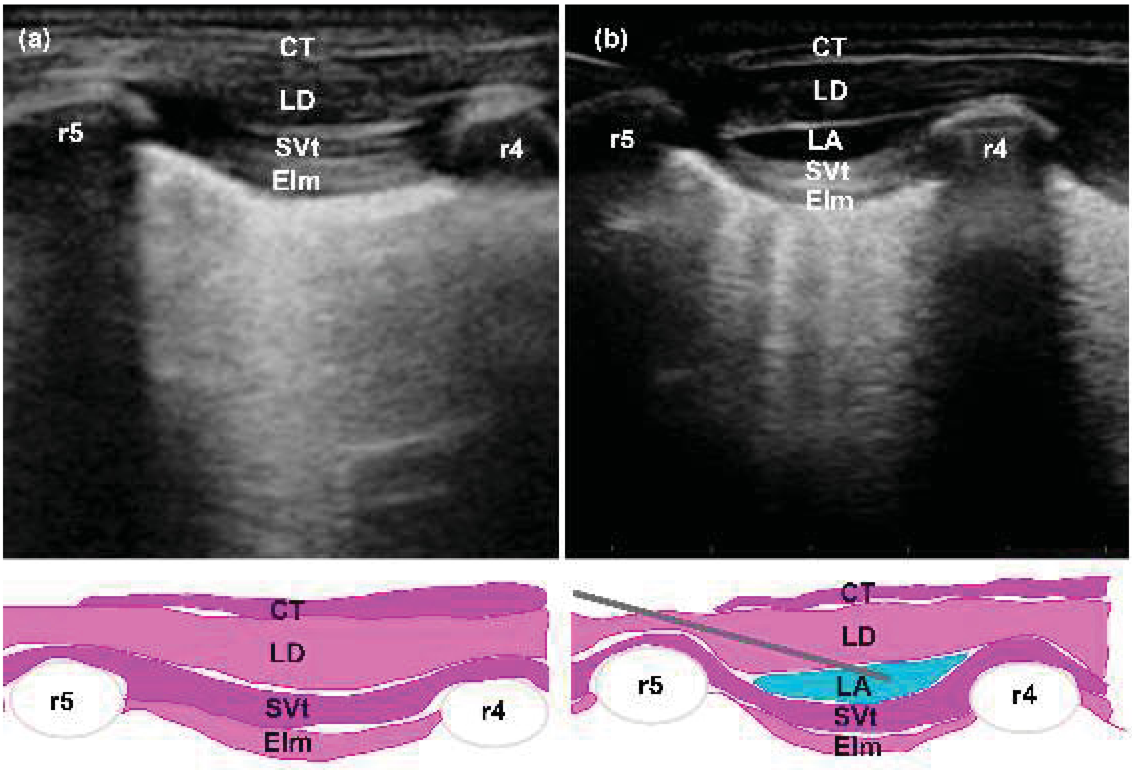

Figure 2 – Ultrasonogram and schematic images obtained during cadaveric SSP block with linear probe postioned perpendicular to the ribs, over the fourth and fifth ribs, at the height of the shoulder joint. a) Muscular layers identified between the 4th and 5th ribs. Muscle layers can be identified by hyperechogenic lines (fascia) separating each muscle. Representative image made from the ultrasound image above. b) Local anesthetic solution with methylene blue visualized by ultrasound in SSP. The solution is seen as an anechoic layer between the fascia of the serratus ventralis thoracis and latissimus dorsi muscles. Representative image made from the ultrasound image above with the gray line showing the needle positioning in the correct fascial plane. Legend: CT, cutaneous trunci muscle; EIm, external intercostal muscle; LA, local anesthetic with methylene blue solution; LD, latissimus dorsi; SVt, serratus ventralis thoracis muscle.

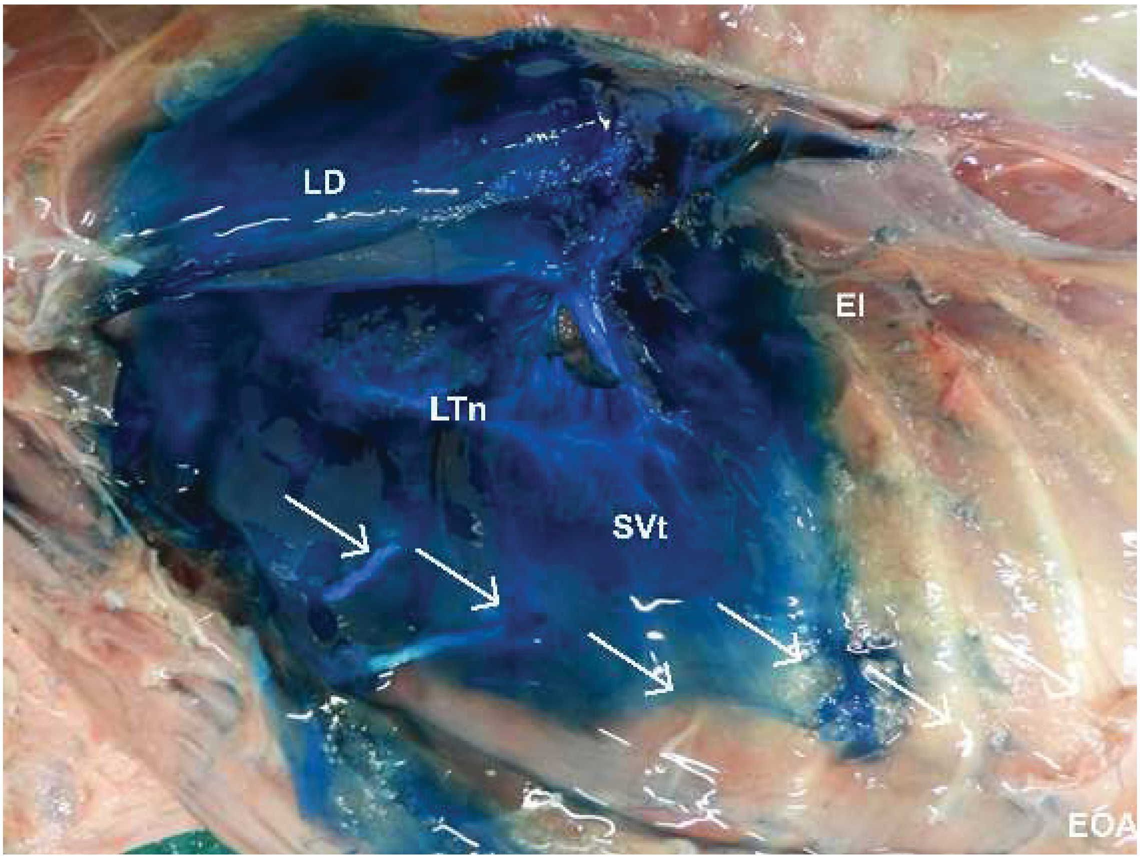

Figure 3 – Dissected dog cadaver showing solution dispersion of G0.6. The superficial serratus plane is stained with methylene blue. There is staining of the lateral cutaneous branches and the long thoracic nerve. Legend: EI, external intercostal muscle; EOA, external oblique abdominal muscle; LD, latissimus dorsi muscle; LTn, long thoracic nerve; SVt, serratus ventralis thoracis muscle; Arrows, intercostobrachial nerve II and III and lateral cutaneous branches of the intercostal nerves IV, to VII.

Table 1. Blue methylene solution dispersion in dog cadavers at the superficial serratus plane block, divided by ribs in the groups 0.3, 0.6 and 1 mL kg^{-1}. Results presented by the number of cadavers stained with the solution with a stained area on the nerve predicted position, followed by the total blocks evaluated in the same group (x/y) with the representative percentage ($p > 0.05$ for all analysis). No significantly statistic difference was found.

Rib Number	G0.3	G0.6	G1
T1	4/8 (50%)	5/9 (55.56%)	7/9 (77.78%)
T2	6/8 (75%)	7/9 (77.78%)	8/9 (88.89%)
T3	7/8 (87.50%)	9/9 (100%)	9/9 (100%)
T4	8/8 (100%)	9/9 (100%)	9/9 (100%)
T5	7/8 (87.50%)	8/9 (88.89%)	9/9 (100%)
T6	4/8 (50%)	5/9 (55.56%)	6/9 (66.67%)
T7	1/8 (12.50%)	1/9 (11.11%)	3/9 (33.33%)
T8	1/8 (12.50%)	0/9 (0%)	2/9 (22.22%)
T9	1/8 (12.50%)	0/9 (0%)	1/9 (11.11%)

5. Chapter Two

Transversus abdominis plane block and superficial serratus plane block for intra and postoperative analgesia in propofol anesthetized bitches undergoing mastectomy

Transversus abdominis plane block and superficial serratus plane block for intra and postoperative analgesia in propofol anesthetized bitches undergoing mastectomy

Authors

Flavio Augusto Vieira Freitag[a] (E-mail: flavio_freitag@hotmail.com)

Amanda Aparecida Mazur dos Santos[a]

Thalise da Silva Gaio[a]

Eloisa Muehlbauer[a]

Jana Eliza Bassetto[a]

Ariele Parecida Ferreira[a]

Juan Carlos Duque Moreno[a] (E-mail: anestesiologiavet@yahoo.com.br)

Authors Affiliation

A. Veterinary Sciences Graduate Program, Department of Veterinary Medicine, Federal University of Paraná. Postal Adress: Rua dos Funcionários 1540, Juvevê, Curitiba – PR, Brazil. CEP 80.035-050.

Correspondence Author:

Juan Carlos Duque Moreno

Department of Veterinary Medicine, Federal University of Paraná. Rua dos Funcionários 1540, Juvevê, Curitiba – PR, Brazil. CEP 80.035-050, Brazil.

Phone number: 55 41 3350-5810

Cellphone: 55 41 9 9173-3606

E-mail: anestesiologiavet@yahoo.com.br

Authors' Contribuitions

FAVF: Study design, acquisition of data, analysis and interpretation of data, preparation of the manuscript.

AAMS: Acquisition of data, analysis and interpretation of data.

TSG: Acquisition of data, analysis and interpretation of data.

EM: Acquisition of data, analysis and interpretation of data.

JEB: Acquisition of data, analysis and interpretation of data.

AAF: Acquisition of data, analysis and interpretation of data.
JCDM: Study design, acquisition of data, analysis and interpretation of data, preparation and critical review of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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5.1. Resumo

Objetivo Avaliar os efeitos analgésicos da associação do bloqueio do plano transverso do abdômen (TAP) e bloqueio do plano serrátil superficial (SSP) no trans e pós-operatório de cães submetidos a mastectomia total unilateral.

Design experimental Estudo clínico controlado, aleatorizado, prospectivo e duplo-cego.

Animais Um grupo de 32 cadelas com tumores mamários

Métodos Os animais foram divididos em quatro grupos (n = 8 cada). Grupo anestesia local (LG), grupo meloxicam (MxG), grupo metadona (MtG) e todos os tratamentos (ATG). Todos os grupos receberam acepromazina (0,03 mg kg^{-1} IM) como medicação pré-anestésica, pacientes de MtG e TG receberam metadona (0,3 mg kg^{-1} IM) associada. MxG e TG, receberam meloxicam (0,1 mg kg^{-1} SC) ao mesmo tempo da medicação pré-anestésica. LG e TG receberam TAP e SSP block com ropivacaína 0,5% (0,3 mL kg^{-1}) em cada ponto, após indução anestésica. Indução e manutenção anestésica foi realizada com propofol. Durante a cirurgia um aumento na FC, *f* e/ou PAS maior que 20% foi tratada com fentanil (2,5 µg kg^{-1} IV). Antes da medicação pré-anestésica e 1, 2, 3, 4, 6, 8, 12, 16, 20 e 24 horas após a extubação, a dor foi avaliada com CMPF-SF e VAS. Para escores de CMPF-SF $\geq$ 6, metadona (0,3 mg kg^{-1} IM). Os dados foram analisados com ANOVA, Kruskal-Wallis, teste de Friedman, teste exato de Fisher. Diferença quando $p <$ 0,05.

Resultados Todos os grupos necessitaram resgate analgésico durante a cirurgia. No período pós-operatório o número de animais resgatados nos grupos MxG, LG, TG e MtG foi de 0, 2, 1 e 3, respectivamente, sem diferenças entre grupos. Contudo, o número total de regates foi maior em MtG (15) do que em MxG (0), LG (3) e TG (1) (p = 0,002). Os escores na CMPS-SF foram maiores em MtG em comparação com MxG, LG e TG, 1, 4, 6 e 8 horas após a extubação (p = 0,016, p = 0,022, p = 0,05, p = 0,023, respectivamente).

Conclusão e relevância clínica SSP e TAP block podem ser utilizados no contexto de protocolos de analgesia multimodal, para fornecer analgesia pós-operatória em cães.

Palavras-chave: Analgesia, anestesia local, ultrassonografia, oncologia, propofol.

5.2. Abstract

Objective To evaluate the intra and postoperative analgesic effects of the transversus abdominis plane block (TAP block) and the superficial serratus plane block (SSP block) in bitches undergoing total unilateral mastectomy.

Study design Controlled, randomized, prospective, blinded clinical study.

Methods Animals were allocated in four groups (*n* = 8) to receive meloxicam (MXG), methadone (MTG), TAP and SSP blocks (LG) and all treatments (ATG). Acepromazine (0.03 mg kg^{-1} IM) was administered as premedication in all groups. Dogs in MTG and TG also received methadone (0.3 mg kg^{-1} IM) and dogs in MXG and TG also received meloxicam (0.1 mg kg^{-1} SC). Dogs in LG and TG received TAP and SSP block with 0.5% ropivacaine (0.3 mL kg^{-1} at each injection point) after anesthetic induction. Anesthesia was induced and maintained with propofol. If increases >20% in HR, f_R and/or SAP were observed in response to surgical stimuli, rescue intraoperative analgesia was performed with fentanyl (2.5 μg kg^{-1} IV). Pain was assessed with the short form of the Glasgow Composite Measure Pain Scale (CMPS-SF) before premedication and at 1, 2, 3, 4, 6, 8, 12, 16, 20 and 24 hours after extubation. Rescue analgesia was performed with methadone (0.3 mg kg^{-1}, IM) when CMPF-SF ≥ 6. Data was analyzed with One-way ANOVA, Kruskal-Wallis, Fishers exact test and Friedman's test. Diference when p <0.05.

Results There were no differences in intraoperative rescue analgesia between groups. At postoperative period the number of animals that receive rescue at MxG, LG, TG and MtG was of 0, 2, 1 and 3 respectively, without difference between the groups. However, the total number of rescues was higher at MtG (15) than in MxG (0), LG (3) and TG (1) (p = 0.002). The CMPF-SR scores were higher in MtG in comparison to MxG, LG and TG at 1, 4, 6 and 8 hours after extubation (p = 0.016; p = 0.022; p = 0.05; p = 0.023 respectively).

Conclusions and clinical relevance SSP and TAP block may be an option to provide intra and postoperative analgesia in bitches undergoing mastectomy.

Keywords balanced anesthesia, surgical oncology, ultrasound-guided regional anesthesia

5.3. Introduction

Total unilateral mastectomy is the most used treatment modality for mammary tumors in dogs (Morris et al. 2000). Mastectomy is considered as an extensive and invasive procedure (Mathews et al. 2000) that may lead to high-levels of stress and pain, increasing the patient morbidity during the perioperative period (Nakagawa et al. 2007).

Local and regional anesthesia can be used as adjuvant techniques to treat acute pain and prevent chronic pain in humans submitted to mastectomy, reducing opioid consumption and the adverse effects associated with these drugs (Bolin et al. 2015). Another positive effect of the use of local anesthesia in cancer surgery is the reduction in the rate of relapses in humans, due apoptotic cancer cell death, inhibition of cancer cell invasion, the reduction of mesenchymal stem cells proliferation and other cellular effects (Kim, 2018). The use of local anesthesia is one of the therapeutic approaches that can be used to promote analgesia for mastectomy in dogs.

The transversus abdominis plane block (TAP block) is an ultrasound-guided technique that provides analgesia of the ventral and lateral abdominal wall, including the skin, mammary gland, subcutaneous tissue, muscles and parietal peritoneum (Schroeder et al. 2011; Castaneda-Herrera et al. 2017). Preliminary studies had shown that the association of TAP block and intercostal nerve block may be useful for intraoperative anti-nociception and postoperative analgesia in dogs submitted to unilateral mastectomy (Portela et al. 2014).

Another fascial plane block guided by ultrasonography is the superficial serratus plane block (SSP block) (Blanco et al. 2013) that has already been described for the pain treatment of mastectomy and post mastectomy pain syndrome in humans (Takimoto et al. 2016; Zocca et al. 2016; Cassi et al. 2017). However, there are no studies of SSP block in dogs, an deep approach of the serratus plane associated with TAP block was used in dogs with promising results (Teixeira et al. 2018).

The objective of this clinical study was to evaluate the intra and postoperative analgesia obtained with the association of SSP and TAP block techniques for total unilateral mastectomy. Our hypothesis was that regional anesthesia techniques would reduce the requirements of intra and postoperative rescue analgesia when compared to groups receiving just an opioid (methadone) or a non-steroidal anti-inflammatory (meloxicam), and dogs receiving the three forms of analgesia would have the lowest pain scores and requirements of rescue analgesia.

5.4. Material and Methods

This study was approved by the local commission on ethics on the use of animals of the Federal University of Paraná – Agricultural Science Sector (CEUA-SCA) protocol number 06/2019. The sample size was calculated using SigmaPlot after the twelve animals were used, considering the pain scores two hours after extubation. To detect a minimum of 2 (point) in the means with an expected standard deviation (3 animals of each groups) of 2.2, with a statistical power of 80% and alpha error of 0,05. A sample size of 28 was needed (7 animals per group), due this one more animal was added in each group.

Animals

Thirty-two adult female dogs, weighing between 4.8 and 26.5 kg, from different breeds, were used in this controlled, prospective, randomized, blinded clinical study. Animals with mammary tumors in which total unilateral mastectomy was indicated, physical ASA status II or III, without metastasis and after owners' written consent were included. Animals with aggressive behavior, blind or deaf, systemic disease or ingestion of NSAIDS, opioids or other pain medications in the last 15 days before the surgery were excluded. All animals were hospitalized at least two hours before the surgery to acclimatize them to the experimental environment.

Total unilateral mastectomy was performed by the same surgeons (AAF) in all patients. Starting with an elliptical incision of skin and subcutaneous tissue, from the first thoracic until the last abdominal mammary gland, with 1-2 cm margin of healthy tissue in all directions. Mammary gland chain is remove by dissection, and vessels and arteries were sutured with 910 polygalactin. After removal subcutaneous suture with 910 polygalactin and skin suture with nylon was performed.

Group Randomization

Dogs were numbered from 1 to 32 and randomized using the Random Sequence Generator tool available at 'random.org' to receive one of four treatments:

- MTG – Methadone Group - premedication with acepromazine (0.03 mg kg^{-1} IM; Acepran 2 mg mL^{-1}; Vetnil, Brazil) and methadone (0.3 mg kg^{-1} IM; Mytedon 10 mg mL^{-1}; Cristália, Brazil);

- MXG – Meloxicam Group - premedication with acepromazine (0.03 mg kg^{-1} IM) and meloxicam (0.1 mg kg^{-1} SC; Flamavet 2 mg mL^{-1}; Agener, Brazil);
- LG – Local Anesthesia Group - premedication with acepromazine (0.03 mg kg^{-1} IM) and TAP + SSP block with 0.5% ropivacaine (0.3 mL kg^{-1} for each block; Ropi 7.5 mg mL^{-1}; Cristália, Brazil) (Ropivacaine was diluted in sterile water to a concentration of 0.5%) after anesthetic induction;
- ATG – All treatments Group - premedication with acepromazine (0.03 mg kg^{-1} IM), methadone (0.3 mg kg^{-1} IM) and meloxicam (0.1 mg kg^{-1} SC); associated with TAP + SSP block with 0.5% ropivacaine (0.3 mL kg^{-1} for each block) after anesthetic induction;

Anesthesia and monitoring

Food and water were withdrawn for 8 and 1 hours, respectively, before the surgery and the procedures were always performed at the morning, beginning at 9 am. After the two hours of adaptation, a blind researcher registered the baseline pain scores and physiologic parameters. After the first evaluation, another veterinary anesthesiologist (JEB) prepared the patients for the surgical procedure. Premedication was administered according to each group and after 15 minutes a venous catheter was placed at the right cephalic vein for drug and fluid administration.

Once the dogs were placed over the surgical table, electrocardiographic trace (ECG) (Digicare Animal Health, LifeWindow™ LW9xVet, Rio de Janeiro – RJ) and systolic blood pressure (SAP) (Parks Medical – 811B, USA) performed in the left thoracic limb, using a 40 to 60% limb circumference size cuff, using the mean of three values as the final SAP, monitoring was started. Pre-oxygenation with a facial mask and a flow of 3 L/min with 100% O_2 was performed by 5 minutes. Anesthesia was then induced with propofol (Propovan 10 mg mL^{-1}; Cristália, Brazil) until the patient lost protection reflex and allow tracheal intubation. Patients received 100% O_2 in a non-rebreathing circuit (Baraka) if body weight was less than 6 kg and in a rebreathing circle system for patients with more than 6 kg. All patients were kept in spontaneous breathing. Anesthesia was maintained with a propofol continuous rate infusion (CRI) of 0.3 mg kg^{-1} min^{-1} and all patients received lactated Ringers solution at 3 mL kg^{-1} h^{-1} during all the surgery. Patients were placed in lateral recumbency to perform the regional anesthesia techniques in LG and ATG groups by JEB.

Anesthetic monitoring included HR, ECG, f_R, mainstream $P_E'CO_2$, esophageal temperature (T) (Digicare Animal Health, LifeWindow™ LW9xVet, Rio de Janeiro – RJ) and SAP (Parks Medical – 811B, USA). Parameters were monitored every 5 minutes, starting before local anesthesia, during local anesthesia (in LG and ATG), until the extubation of the patient. Surgical procedure would only begin after 15 minutes of the end of the local block or after the time the block was supposed to do for MXG and MTG (around 5 minutes). The dogs were placed in dorsal recumbency, and surgical antisepsis was started, in this moment the same blind researcher (FAVF) would come to the surgical room and begin the evaluations. During surgery SAP was kept > 90 mmH, in case of hypotension, one fluid bolus 10 mL kg^{-1} of lactated ringer solution in 15 minutes, was given to the patient, in case the pressure did not return to normal values ephedrine 0.05 mg kg^{-1} IV (MARCA) was given. $P_E'CO_2$ was kept in 35 to 45 mmHg.

Anesthetic deep was evaluated every five minutes, it was desired the patients stayed in stage III, plane two (light to moderate surgical anesthetic plane). In case the patient presents sing of superficialization (positive palpebral reflex, central position of the eye bulb, mydriasis, mandibular tonus) propofol infusion was increased in 0.05 mg kg^{-1} min^{-1} if the patient presents deep anesthetic plane (mydriasis, central position of the eye bulb, cardiovascular depression, absence of gore reflex) the propofol infusion was decreased in the same dose. Propofol CRI was discontinued when the surgeon starts the last skin stiches. Surgical bandage was made in all patients, and they were referred to the same room they were evaluated before the surgery.

TAP and SSP block

With the dog in lateral recumbency, with the side to be operated facing up, surgical antisepsis was performed in all lateral wall of the thorax and abdomen. The same veterinary anesthesiologist started the local anesthetic procedure with the SSP block.

A linear transducer of (7.5 – 12 MHz) (LA523, Esaote MyLab Vet Gold, Esaote, Italy) was placed perpendicular to the ribs, over the fourth and fifth ribs, at the lever of the shoulder join. The identification of the thoracic wall muscles with ultrasound was proceeded until the clear view of the cutaneous trunci, latissimus dorsi, serratus ventralis thoracis and external intercostal muscles. A 20 G 3.5' Tuohy needle (BD Perisafe™) was introduced in an in-plane, caudocranial guidance until the needle tip reach the fascial plane between the latissimus dorsi and serratus ventralis thoracis (Figure 1). To confirm the needle placement, a three-way stopcock was connected by the end of the Tuohy needle, and a test dose of 1 mL of saline solution was injected. The correct position was confirmed if an anechoic ‘bubble’ was seen in the fascial plane between the two muscles, and the injection of 0.3 mL kg^{-1} of 0.5% ropivacaine was performed.

By the end of SSP block, with the same transducer and Tuohy needle, it was continued with the TAP block. The ultrasound transducer was positioned parallel to the ribs, at the midpoint between the last rib and the anterior margin of the iliac crest, with the marker dorsally and at the same level of the SSP block. The muscles of the abdominal wall layer were identified (external abdominal oblique, internal abdominal oblique and transversus abdominis muscles), and with an in-plane approach, the needle was inserted until the tip reach the fascial plane between internal abdominal oblique and transversus abdominis muscles (Figure 1). The confirmation was realized in the same manner of the SSP block, and if the needle placement was correct another 0.3 mL kg^{-1} of 0.5% ropivacaine were injectated. The time from the beginning of the thoracic wall ultrasound identification until the end of TAP block injection was timed in seconds.

Evaluation of intra and postoperative analgesia

Surgical analgesia was assed based on the cardiovascular and respiratory changes secondary to surgical stimulation. Nociceptive response was treated when HR, f_R and/or SAP increased more than 20% from the anesthetized baseline parameters, that were obtained during the first 10 minutes after anesthetic induction of evaluation before any stimulation (anesthetic blockade, or surgery). The blind evaluator, would always check anesthetic depth first, and in the cases the anesthetic deep was not the problem, 2.5 μg kg^{-1} of fentanyl (Fentanest 0.05 mg mL^{-1}; Cristália, Brazil) was administered intravenously, and surgeons need to wait for 5 minutes before the continuation of the surgery. The number of anesthetic rescues during the surgery, and physiological parameters were recorded for further analysis.

After the end of the surgery the patients stayed in a room, in cages, without contact to other people or animals for pain, sedation and behavior evaluation by the blind observer (FAVF) for 24 hours, after extubation. Evaluation was performed at 1, 2, 3, 4, 6, 8, 12, 16, 20 and 24 hours after extubation in all patients. Just after the last evaluation home prescription medication started. Patients returned after 15 days for suture removal.

Before any contact the behavior of the animals was observed while they remained in the cage. After that, the researcher called them by their names and open the cages’ door. Patients were set free of the cage to walk for a minute. Once in lateral recumbency, with the operated side facing up, digital pressure was applied by the observer at three points over the surgical incision (in the middle of the incision, in the middle of the thoracic incision and in the middle of the abdominal incision). Patients were taken to the yard to walk, and were observed for urination and defecation. Dry food mixed with can food and water was available at the cages and at each time of evaluation it was evaluated if the animals had eaten.

Postoperative pain was evaluated by the Short-form Glasgow Composite Measure Pain Scale (CMPS-SF) and by the visual analog scale (VAS), marking a point in a 10 cm line. Analgesic rescue was performed with methadone (0.3 mg kg^{-1} IM) if CMPS-SF scores $\geq 6/24$. In case of analgesic rescue, the patient was observed one hour after and new dose of methadone was administered if necessary. If after 4 consecutive rescues with methadone the CMPS-SF scores remained $\geq 6/24$, in the next hour ketamine (1 mg kg^{-1} IM; Ketamina Agener 100 mg mL^{-1}; Agener, Brazil) was associated to methadone; and if at the next evaluation the pain scores remained $\geq 6/24$ dipyrone (25 mg kg^{-1} IM; Analgex V 500 mg mL^{-1}; Agener, Brazil) was administered alone. Animals that received analgesic rescues, were kept in the evaluation of the study, and scores obtained in the times of evaluation were used in further analysis. The number of animals requiring rescue analgesia, the number of analgesic rescues, and the total dose of methadone administered over 24 hours were recorded.

Statistical Analysis

Normal distribution of data was assessed using the Shapiro-Wilk test. For between-groups comparisons One-Way ANOVA followed by Tukey test were used for normally distributed data and results are expressed as mean ± standard deviation. Non-normally distributed data was analyzed by Kruskal-Wallis followed by Tukey test and presented as median (range). For comparisons within groups with baseline Repeated measures ANOVA and Friedman's test analysis for normal and non-normally distributed data respectively were used followed by the Dunn's test for *pos hoc* comparison. To compare occurrence (analgesic rescue, number of animals) between groups it was used the Exact Fishers test. Differences were considered significant when $p < 0.05$. All statistical tests were performed using Sigma Plot for Windows 12.0 (Systat, CA, USA). Figures with statistical information were generated using the free R 3.5.3 software (R Foundation for Statistical Computing, Austria).

5.5. Results

Intraoperative results are show in table 1. From the total four animals (1 MXG, 1 MTG and 2 LG) presented hypotension (SAP < 90 mmHg), and all of them were treated with 10 mL kg^{-1} of lactated ringer solution in 15 minutes, one of them needed ephedrine 0.05 mg kg^{-1} IV, after the fluid bolus to treat hypotension.

There were no differences in demographic data, total dose of propofol for induction and maintenance of anesthesia, time to perform TAP and SSP block (LG and ATG), time of surgery, anesthetized time (from induction until extubation), recovery time (from the end of administration of anesthetic agents until extubation and sternal recumbency). All the data is summarized at tables 2 and 3.

There were no differences in the number of animals requiring intraoperative rescue, total number of rescues, median number of rescues per animal, total dose of fentanyl and time from the beginning of the surgery until the first analgesic rescue between groups. Similarly, during the 24 h postoperative period the number of animals requiring analgesic rescue, median number of rescues per animal, total dose of methadone used and the time until the animals eat did not differ between groups (Table 3). The total number of rescues was higher in MTG than in all the other groups ($p = 0.002$). Three animals in MTG had CMPS-SF scores ≥ 6 even after five doses of rescue methadone, and one dose of ketamine, the effective analgesia (CMPS-SF scores ≤ 6) was attained only after they received dipyrone (25 mg kg^{-1}, IM). Time for the first analgesic rescue was 6h for animals in LG (2) and 1h for animals in MTG (3) and ATG (1). Except from the animal at TG, all the other animals that received post-operative analgesic rescue, received at least one analgesic rescue during the surgery. Three animals did not eat in the hospitalization period, two from MTG and one from LG.

Results obtained at CMPS-SF and VAS are represented at boxplot graphics 1 and 2 respectively. All this scores were evaluated as non-parametric data. At CMPS-SF statistical difference was observed in MTG higher values when compared among groups at T1, T4 and T8 ($p = 0.016$; $p = 0.022$; $p = 0.05$; $p = 0.023$ respectively), at T6 $p = 0.053$ (almost statistical difference). When CMPS-SF was evaluated within each group over time, comparing to the baseline, just MTG presented difference at T1 (higher values). VAS results, did not show statistical difference between groups or over time within groups.

No complications related to the techniques were observed in the 24 hours' period or until the day of suture removal.

5.6. Discussion

The results of this study suggest that the association of the SSP and TAP block techniques can be used as a part of multimodal analgesic approaches in dogs submitted to total unilateral mastectomy. To the authors knowledge this is the first time the TAP and SSP block are associated and used for dogs undergoing total unilateral mastectomy with general anesthesia with propofol. The combination of the techniques are easy to perform and take a small amount of time (2 to 6 minutes). Also the association was based on preliminary not published studies, where the techniques as proposed here with 0.3 mL kg^{-1} can block lateral cutaneous branches from T1 up to T9 with SSP block and L1 to L3 with TAP block, that corresponds to the main innervation of the mammary gland chain in dogs (T4 to T7 and L1 to L3) (Evans & DeLahunta, 2013).

Local anesthesia, opioids and NSAIDs are described in the literature for pain management in dogs for several surgical conditions, including mastectomy (Nakagawa et al. 2007; Portela et al. 2014; Uscagueti et al. 2016). It's discussed by some authors the importance of multimodal anesthesia in huge surgical procedures (Minto et a. 2013; Uscagueti et al. 2016), but the real needs of pain medications in dogs undergoing total unilateral mastectomy is confusing due the amount of drugs used and the different types of pain and nociceptive evaluation performed. Because of this the CMPS-SF was used as the gold standard for pain evaluation at the postoperative period, as it is already validated for using in dogs (Reid et al. 2007), and the analgesic protocols were tested individually and combined (Local anesthesia, NSAID and opioid).

In this study the induction and maintenance dose did not differ statistically between the treatment groups. Induction dose stayed around 3 to 5 mg kg^{-1} for animals, that is near the propofol dose described in the literature (Short & Bufalari, 1999). It was expected that the individuals who received methadone as premedication would use lower doses of propofol to anesthetic induction, however this was not observed in our study. Also propofol maintenance dose did not resent statistical significant difference between the treatment groups, with a range of maintenance dose from 16 to 24 mg kg^{-1} h^{-1}, that would represent around 0.25 to 0.35 mg kg^{-1} min^{-1}, that corroborate to the previous literature (Short & Bufalari, 1999).

Together with propofol, local anesthesia has been extensively used in medicine to promote analgesia, reduce general anesthetic doses or use (when possible) and reduce neuroendocrine surgery-induced response and immunosuppression in oncologic patients (Kim, 2018). In our study the TAP associated with SSP block with 0.5% ropivacaine were used as the regional anesthesia technique. TAP block was already reported in two studies as being used with serratus plane block or intercostal nerve block, to promote analgesia to mastectomy in dogs (Portela et al. 2014; Teixeira et al. 2018), both papers conclude that in the time patients were evaluated, the regional techniques used were useful for pain control. However, both studies used bupivacaine, and TAP and serratus plane block were different from the techniques proposed here, with TAP block being performed in a two-points approach, and serratus being applied at the deeper fascial plane (between serratus ventralis thoracis and external intercostal muscle) in two-point injection. Also no nociceptive rescues were needed (Teixeira et al. 2018), when 1.8 V% Isoflurane was used, and mean arterial pressure and HR were used as trigger values.

Ropivacaine was used due the positive results in cancer recurrence obtained at the medicine (Bajwa et al. 2015), less intense and shorter motor blockade, long lasting analgesic duration (6 to 8 hours) with lower toxicity when compared to bupivacaine (McClure 1996).

Opioids still play an important role in analgesic management of dogs, being the more traditional way to prevent or treat perioperative pain (MacFarlane, 2018). From the literature review performed, methadone was used in at least four studies as premedication for dogs submitted to mastectomy (Portela et al. 2014; Uscagueti et al. 2016; Uscagueti et al. 2017; Teixeira et al. 2018). Some of the findings from this studies included that with local anesthesia methadone had a good analgesia (Portela et al. 2014; Teixeira et al. 2018), resulted in reduced anesthetic requirement when given in higher dose (0.5 mg kg^{-1}) at the pre and intraoperative period (Uscagueti et al. 2017) and was better than tramadol but not completely adequate for pain control (Uscagueti et al. 2016). However, recent studies show that opioid has a guilty participation in the development of metastasis (Trapaidze et al. 2000; Cata et al. 2011). This conflicting information of the studies, the bad effects of opioids in cancer, and the opioid-sparing working task force (Muir et al. 2018) lead us to study the real analgesic function of methadone in the total unilateral mastectomy in dogs.

MXG showed good results at postoperative analgesia. However, oncology patients are usually geriatric patients, leading to a reduction in drug clearance capacity and probably renal or hepatic dysfunction associated, this makes them more susceptible to NSAID toxicity, and alternative analgesic techniques such as local anesthesia must be considered (Lascelles et al. 2005; Hughes, 2008).

It was expected that the groups with regional anesthesia would need lees or no intraoperative nociceptive analgesic rescue, with less propofol consumption, and less or no postoperative analgesic rescue. The first rescue was almost always at the beginning of the surgery, when the skin incision was performed in the majority of the animals. Probably this is because one of the peeks of nociception during the procedure is the skin incision (MacFarlane, 2018). This suggests that the analgesic protocols presented here do not abolish completely the nociception stimulation during total unilateral mastectomy. However, since the baseline parameters that were used to evaluate nociception stimulation were obtained in the first 10 to 15 minutes immediately after the patient induction with propofol, and it's expected that propofol lead to a respiratory and cardiovascular depression after induction, the baseline parameters may be lower than the actual parameters, and some of the nociceptive analgesic rescues could be not necessarily needed (Sano et al. 2003; Sams et al. 2008).

At the postoperative period of 24 hours, MTG showed the worst result, with the higher number of analgesic rescues ($p = 0.002$), showing that the single use of 0.3 mg kg^{-1} methadone as analgesic therapy for total unilateral mastectomy is not sufficient. This result corroborates findings from Uscagueti et al. (2016), suggesting the occurrence of opioid induced hyperalgesia, as previously reported in humans (Yi & Pryzbylkowski, 2015) or higher preemptive doses may be used (Uscagueti et al. 2016). All individuals rescued in MTG received at least five consecutive methadone doses, and CMPS-SF just returned to values lower than 6 after the administration of dipyrone. According to Sleeckx et al. (2011) total unilateral mastectomy causes mainly inflammatory pain, this explains why groups receiving the NSAID had low pain scores and reinforces the importance of the use of NSAIDs in surgical procedures when patients are able to use them.

Two animals in LG received analgesic rescue, both of them at T6 and one of them received a second rescue at T12. This make sense, since the effects of 0.5% ropivacaine were reported to last between 6 and 8 hours (Sakonju et al. 2009). The second rescue 6 hours later in one animal coincided with the end of effective analgesia of methadone in dogs (Murrell, 2011).

On the other hand, at ATG just one animal and one rescue was performed at 1 hour after extubation, with a CMPF-SF score of 6, this animal did not receive analgesic rescue during surgery, and this score could be just a find, or individual variation that is expected to happen (Lush & Ijichi, 2018).

Evaluation between among showed statistical differences between MTG and the other three groups at T1, T4 and T8, that matched with the higher number of analgesic rescues in this group.

When each group was compared to the baseline evaluation, just MTG at T1 presented statistical significance that was when the major number of rescues was performed, with the higher Glasgow scores obtained. As showed in figure 1, pains scores increase after surgery, but start decreasing up to 8 to 12 hours after, and then remain stable. The same tendency was observed in other studies involving mastectomy in dogs (Teixeira et al. 2013; Crociolli et al. 2015; Wang et al. 2017). However, no direct explanation was given by the authors.

Although VAS pain scores had increased after surgery in all groups, MTG showed a tendency to higher values than other groups, similar to CMPS-SF scores. In all groups around 8 hours after extubation, the scores tend to be more stable, and lower when compared to the ones after surgery, even for animals that did not receive any post-operative analgesic rescue.

Time for the patients return to eat after surgery, did not differ between the groups. However, is seems that patients that had benefit from local anesthesia (LG and ATG) tends to eat early then when compared to MXG and MTG. Even that this is not evaluated directly, the appetite has relation with pain in dogs and cats (Downing, 2011).

As limitations of this study, we can mention the number of animals, when compared to human studies. However, this number had a statistical power of 80%, and is similar to studies in veterinary medicine, with groups from 6 to 10 animals each. And the power was calculated used CMPS-SF scores and not the number of rescues or propofol doses and this may change the sample needed. The use of Doppler as the SAP and not invasive pressure that is the gold standard for this parameter. The decision to kept the animals after analgesic rescue could influenced the scores, and this can be a limitation of the study. Another point is that not all combinations were tested in this study, such as meloxicam with methadone or meloxicam with local anesthesia or local anesthesia and methadone, and different combinations can bring different results, but due the number of animals available and the main objective to test the TAP and SSP association and the clinical protocol commonly used (NSAID + opioid + local anesthesia) just this groups were studied.

Based on our results, the association of SSP and TAP block may be used as part of multimodal analgesia for intra and postoperative period option for total unilateral mastectomy in dogs. This technique can be combined to other analgesic techniques or as a safer option to geriatric patients that cannot use NSAID. More studies with SSP and TAP block should be use to other surgical procedures for better understanding of analgesic effects in dogs, and with other combination of anesthetic protocols.

5.7. References

Bajwa SJS, Anand S, Kaur G (2015) Anesthesia and cancer recurrences: The current knowledge and evidence. Journal of Cancer Research and Therapeutics 11, 3, 528 – 534.

Bitti FS, Campagnol D, Rangel JPP et al. (2017) Effects of three methadone doses combined with acepromazine on sedation and some cardiopulmonary variables in dogs. Veterinary Anaesthesia and Analgesia 44, 237 – 245.

Blanco R, Parras T, McDonnell JG, Prats-Galino A (2013) Serratus plane block: a novel ultrasound-guided thoracic wall nerve block. Anaesthesia 68, 1107-1113.

Bolin RD, Harvey NR, Wilson SH (2015) Regional anesthesia for breast surgery: Techniques and Benefits. Current Anesthesiology Reports 5, 217 – 224.

Cassi LC, Biffoli F, Francesconi D et al. (2017) Anesthesia and analgesia in breast surgery: the benefits of peripheral nerve block. European Review for Medical and Pharmacological Sciences 21, 1341-1345.

Castaneda-Herrera FE, Buritica-Gaviria EF, Echeverry-Bonilla DF (2017) Anatomical evaluation of the thoracolumbar nerves related to the transversus abdominis plane block technique in the dog. Anatomia Histologia Embryologia 46, 373 - 377.

Cata JP, Gottumukkala V, Sessler DI (2011) How regional analgesia might reduce postoperative cancer recurrence. European Journal of Pain Supplements 5, 345 – 355.

Chevallier DL, Slingsby L, Murrell JC (2018) Randomized clinical trial comparing clinically relevant sedation outcome measure in dogs after intramuscular administration of medetomidine in combination with midazolam or butorphanol for routine diagnostic imaging procedures. The Veterinary Journal 239, 30 – 34.

Crociolli GC, Cassu RN, Barbero RC et al. (2015) Gabapentin as an adjuvant for postoperative pain management in dogs undergoing mastectomy. Journal of Veterinary Medical Science 77, 8, 1011-1015.

Downing R (2011) Pain management for veterinary palliative care and hospice patients. Veterinary Clinics of North America: Small Animal Practice 41, 3, 531 – 550.

Evans HE, Lahunta A. *Miller's Anatomy of the Dog*. 4. ed. St. Louis: Saunders-Elsevier, 2013.

Hughes JML (2005) Anaesthesia for the geriatric dog and cat. Irish Veterinary Journal 61, 6, 380-387.

Kim R (2018) Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence. Journal of Translational Medicine 16, 8, 1 – 13.

Lascelles BDX, McFarland JM, Swann H (2008) Guidelines for safe and effective use of NSAIDs in Dogs. Veterinary Therapeutics 6, 3, 237-251.

Lush J, Ijichi C (2018) A preliminary investigation into personality and pain in dogs. Journal of Veterinary Behavior 24, 62 – 68.

MacFarlane P (2018) Managing perioperative pain in dogs and cats. In Practice 40, 130 – 140.

Mathews KA (2000) Pain assessment and general approach to management. Veterinary Clinics of North America: Small Animal Practice 41, 531 – 550.

McClure JH (1996) Ropivacaine. British Journal of Anaesthesia 76, 300-307.

Minto BW, Rodrigues LC, Stegall PVM et al. (2013) Assessment of postoperative pain after unilateral mastectomy using two different surgical techniques in dogs. Acta Veterinaria Scandinavica 55, 1 - 4

Morris JS, Bostock DE, Mcinnes EF et al. (2000) Histopathological survey of neoplasms in flat-coated retrievers, 1990 to 1998. The Veterinary Record 147, 291 – 295.

Muir W, Berry J, Boothe DW et al. (2018) Opioid-Sparing Pain therapy in animals: Working Task Force.

Murrell J (2011) Clinical use of methadone in cats and dogs. Companion Animal 16, 56 – 61.

Nakagawa K, Miyagawa Y, Takemura N et al. (2007) Influence of preemptive analgesia with meloxicam before resection of the unilateral mammary gland on postoperative cardiovascular parameters in dogs. Journal of Veterinary Medical Science 69, 9, 939 – 944.

Portela DA, Romano M, Briganti A (2014) Retrospective clinical evaluation of ultrasound guided transverse abdominis plane block in dogs undergoing mastectomy. Veterinary Anesthesia and Analgesia 41, 319-324.

Reid J, Nolan AM, Hughes JML et al. (2007) Development of the short-form Glasgow Composite measure pain scale (CMPS-SF) and derivation of and analgesic Intervention score. Animal Welfare 16,97 – 104.

Retsky M, Rogers R, Demicheli R et al. (2012) NSAID analgesic ketorolac used perioperatively may suppress early breast cancer relapse: particular relevance to triple negative. Breast Cancer Research and Treatment 134, 881 – 888.

Sakonju I, Maeda K, Maekawa R et al. (2009) Relative nerve blocking proprieties of bupivacaine and ropivacaine in dogs undergoing brachial plexus block using a nerve stimulator. Journal of Veterinary Medical Science 71, 10, 1279 – 1284.

Sams L, Braun C, Allman D et al. (2008) A comparison of the effects of propofol and etomidate on the induction of anesthesia and on cardiopulmonary parameters in dog. Veterinary Anaesthesia and Analgesia 35, 488 – 494.

Sano T, Nishimura R, Mochizuki M et al. (2003) Clinical usefulness of propofol as an anesthetic induction agent in dogs and cats. Journal of Veterinary Medical Science 65, 5, 641 – 643.

Schroeder CA, Snyder LB, Tearney CC et al. (2011) Ultrasound-guided transversus abdominis plane block in the dog: an anatomical evaluation. Veterinary anaesthesia and analgesia 38, 267-271.

Short CE, Bufalari A (1999) Propofol Anesthesia. Veterinary Clinics of North America: Small Animal Practice 29, 3, 747 – 778.

Sleeckx N, Rooster H, Kroeze EJBV et al. (2011) Canine mammary tumors, an Overview. Reproduction in Domestic Animals 46, 1112 – 1131.

Takimoto K, Nishijima K, Ono M (2016) Serratus plane block for persistent pain after partial mastectomy and axillary node dissection. Pain Physician 19, 481 – 486.

Teixeira RCR, Monteiro ER, Campagnol D et al. (2013) Effects of tramadol alone, in combination with meloxicam or dipyrone, on postoperative pain and the analgesic requirement in dogs undergoing unilateral mastectomy with or without ovariohysterectomy. Veterinary Anaesthesia and Analgesia 40, 641-649.

Teixeira LG, Pujol DM, Pazzim AF et al. (2018) Combination of Transversus abdomens plane block and Serratus plane block anesthesia in dogs submitted to mastectomy. Pesquisa Veterinária Brasileira 38, 2, 315-319.

Trapaidze N, Gomes I, Cvejic S et al. (2000) Opioid receptor endocytosis and activation of MAP kinase pathway. Molecular Brain Research 76, 220 – 228.

Uscagueti RAR, Tiosso C, Moro JV et al. (2016) Pre-emptive methadone or tramadol analgesia for mastectomy and ovariohysterectomy in bitches. Revista Colombiana de Ciencias Pecuarias 30, 39-47.

Uscagueti RAR, Feliciano MAR, Tiosso CF et al. (2017) Comparative Evaluation of Methadone Administration at Different Periods in Bitches Undergoing Mastectomy. Pakistan Veterinary Journal 37, 2, 345-349.

Wang HJ, Chang SC, Lee WM et al. (2017) Comparison of Onsite Infiltration and Constant Rate Infusion for Postoperative analgesia in dogs with Mammary Tumors Undergoing bilateral radical mastectomy and ovariohysterectomy. Taiwan Veterinary Journal 43,3, 177 – 183.

Yi P, Pryzbylkowski P (2015) Opioid induced hyperalgesia. Pain Medicine 16, S32 – S36.

Zocca JA, Chen GH, Puttanniah VG et al. (2017) Ultrasound-Guided Serratus Plane Block for Treatment of Postmastectomy Pain Syndromes in Breast Cancer Patients: A Case Series. Pain Practice 17, 1, 141-146.

5.8. Figures and Tables

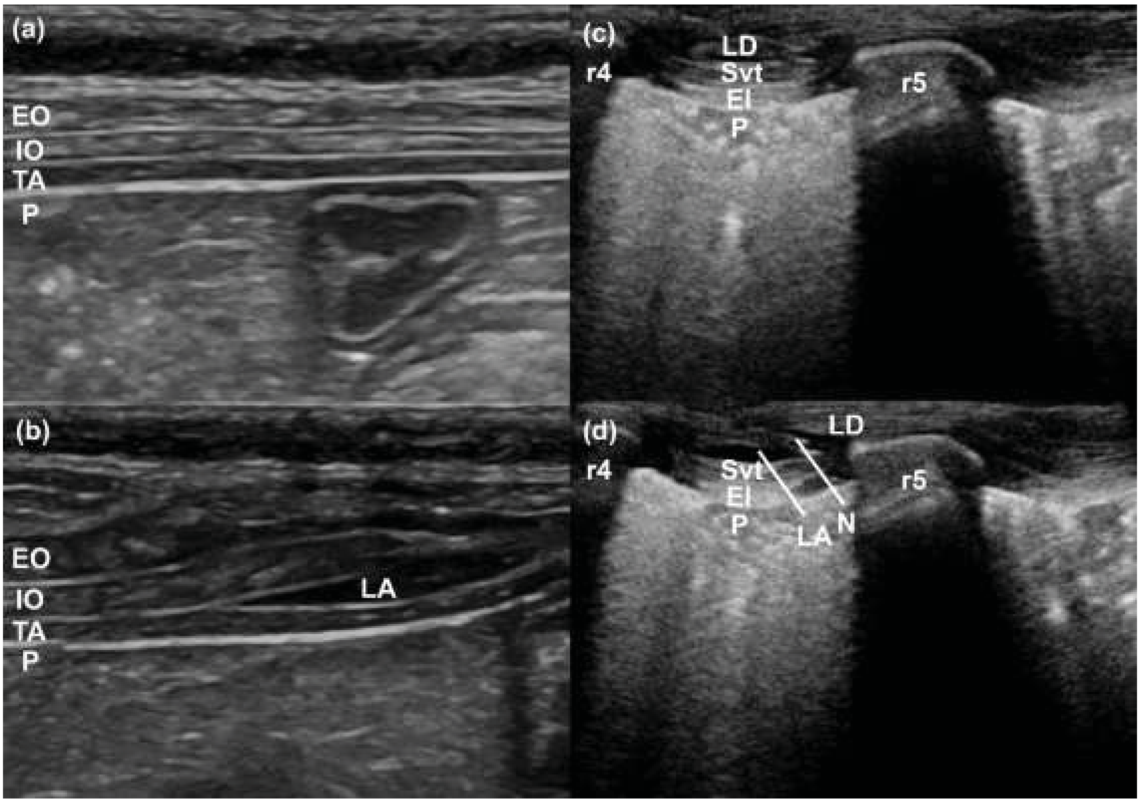

Figure 1. Ultrasound images of transversus abdominis plane (TAP) and superficial serratus plane (SSP) block in a dog submitted to total unilateral mastectomy. TAP block images were obtained with a linear probe, positioned parallel to the ribs, in the midway between the last rib and the anterior margin of the iliac crest, with the marker dorsally at the level of the shoulder joint. SSP block images were performed with the same transducer and at the same level, but with the probe perpendicular to the ribs, over the fourth and fifth ribs in a caudo-cranial in-plane approach. Both techniques were performed with a 20 G Tuohy Needle. a) Muscular layers of the abdominal wall involved in the TAP block technique identified. b) Local anesthetic solution in the TAP, visualized by ultrasound between TA and IO. c) Muscular layers of the thoracic wall involved in SSP technique, visualized by ultrasonography. d) Local anesthetic solution in the SSP, visualized by ultrasound between Svt and LD. Legend: EI, external intercostal muscle; EO, external oblique abdominal muscle; IO, internal oblique abdominal muscle; LA, local anesthetic solution of 0.5% ropivacaine at TAP and SSP block; LD, latissimus dorsi; N, Tuohy needle; P, peritoneum at images a and b, and pleura at c and d images; r4 and r5, fourth and fifth ribs; Svt, serratus ventralis thoracis muscle; TA, transversus abdominis muscle;

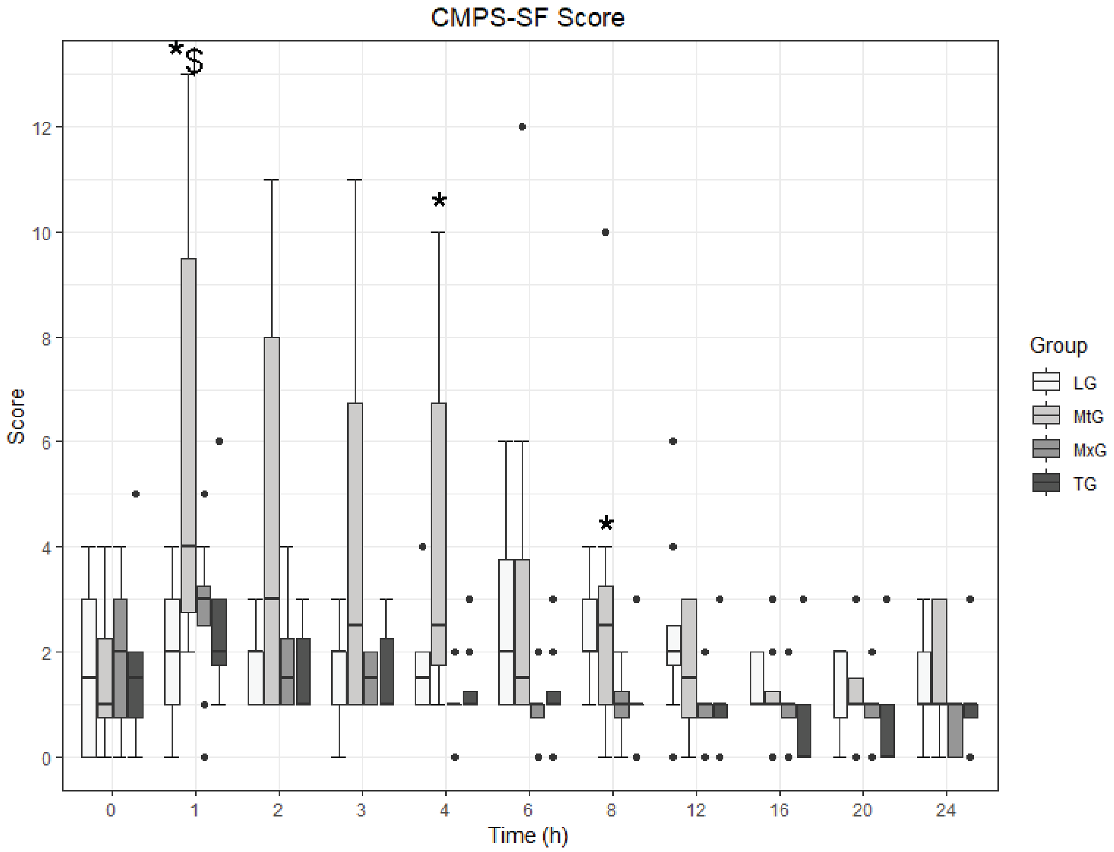

Figure 2. Post-operative pain score evaluation with Short-form Glasgow Composite Measure Pain Scale (CMPS-SF) in 32 dogs undergoing total unilateral mastectomy under general anesthesia with propofol in four different analgesic treatment groups. Superficial serratus plane block with transversus abdomins plane block (LG, n = 8), meloxicam groups (MxG, n = 8), premedication methadone group (MtG, n = 8) and the association of all treatment groups (ATG, n = 8). Scores were evaluated before surgery (0), and 1, 2, 3, 4, 6, 8, 12, 16, 20, 24 hours after extubation. Data are graphically displayed in boxplot. The box upper and lower limits represent the 25th and 75th quartiles of the data, with the line representing the median value. The whiskers extend from 1.5 times the inter-quartile range for hinge to the smallest and largest value with the dots represent the outliers from each group that do not are considered in the whisker extension formula. $^{*}p < 0.05$ between the groups; $^{\$}p < 0.05$ within the same group compared with baseline.

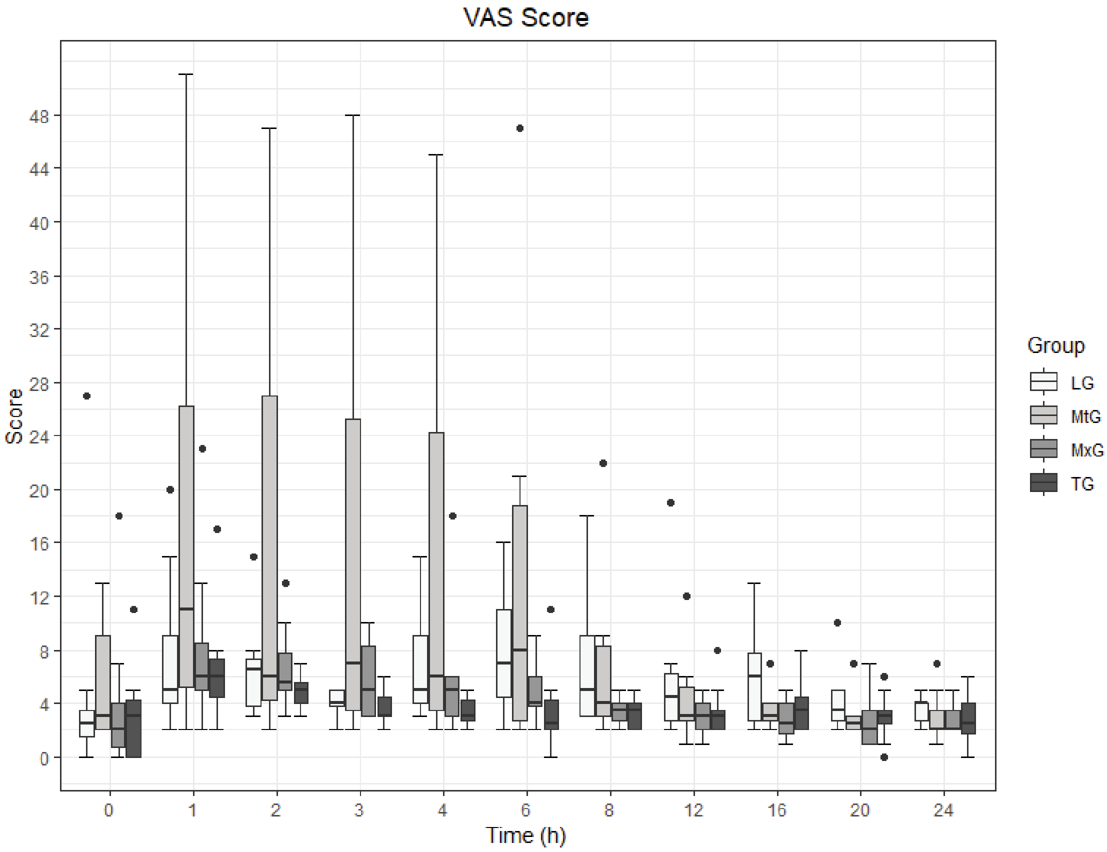

Figure 3. Post-operative pain score evaluation with visual analog scale (VAS) in 32 dogs undergoing total unilateral mastectomy under general anesthesia with propofol in four different analgesic treatment groups. Superficial serratus plane block with transversus abdomins plane block (LG, *n* = 8), preemptive meloxicam groups (MxG, *n* = 8), premedication methadone group (MtG, *n* = 8) and the association of these three techniques groups (TG, *n* = 8). Scores were evaluated before surgery (0), and 1, 2, 3, 4, 6, 8, 12, 16, 20, 24 hours after extubation. Data are graphically displayed in boxplot. The box upper and lower limits represent the 25th and 75th quartiles of the data, with the line representing the median value. The whiskers extend from 1.5 times the inter-quartile range for hinge to the smallest and largest value. The dots represent the outliers from each group that do not are considered in the whisker extension formula.

Table 3. Physiologic parameters mesuared before the surgery, during the incision, during the beginning of incision suture and at the end of the procedure. Different superscript letter within the same collums means the different mean values in the paired analysis between different times and baseline parameters in the same group. Different numbers in the same line means for significant differene ($p < 0.05$) among groups at the same time and parameter. The p value was obtained in the significant analysis ($p = 0.001$; $p = 0.024$; $p < 0.001$ for HR, SAP and T paired anaylsis of LG); ($p < 0.001$ for paired T analysis of MTG, MXG and ATG); ($p = 0.035$ for SAP at incision time among the groups).

Parameter	Evaluation Time	Group			
		LG	MTG	MXG	ATG
HR (bpm)	Baseline	115 ± 9^{a1}	121 ± 24^{a1}	119 ± 22^{a1}	132 ± 27^{a1}
	Incision	116 ± 10^{a1}	125 ± 25^{a1}	115 ± 21^{a1}	134 ± 33^{a1}
	Suture	105 ± 15^{a1}	115 ± 18^{a1}	113 ± 26^{a1}	136 ± 28^{a1}
	End	129 ± 23^{b1}	128 ±22^{a1}	134 ± 40^{a1}	137 ± 34^{a1}
SAP (mmHg)	Baseline	96 ± 11^{a1}	99 ± 15^{a1}	112 ± 19^{a1}	122 ± 32^{a1}
	Incision	97 ± 12^{a1}	101 ± 14^{a1}	117 ± 20^{a2}	120 ± 22^{a2}
	Suture	95 ± 15^{a1}	100 ± 19^{a1}	122 ± 27^{a1}	114 ± 28^{a1}
	End	108 ± 15^{b1}	109 ± 19^{a1}	127 ± 28^{a1}	118 ± 23^{a1}
f_R (mpm)	Baseline	10 ± 7^{a1}	14 ± 4^{a1}	16 ± 12^{a1}	19 ± 11^{a1}
	Incision	11 ± 5^{a1}	13 ± 10^{a1}	21 ± 19^{a1}	11 ± 7^{a1}
	Suture	13 ±11^{a1}	18 ± 12^{a1}	27 ± 23^{a1}	14 ± 13^{a1}
	End	17 ± 10^{a1}	17 ± 10^{a1}	12 ± 6^{a1}	15 ± 4^{a1}
PE'CO_2 (mmHg)	Baseline	37 ± 9^{a1}	36 ± 8^{a1}	37 ± 11^{a1}	36 ± 10^{a1}
	Incision	38 ± 10^{a1}	35 ± 8^{a1}	38 ± 8^{a1}	45 ± 12^{a1}
	Suture	44 ± 11^{a1}	37 ± 11^{a1}	41 ± 9^{a1}	41 ± 6^{a1}
	End	34 ± 5^{a1}	37 ± 12^{a1}	37 ± 9^{a1}	42 ± 11^{a1}
T (°C)	Baseline	37.7 ± 0.4^{a1}	37.7 ± 0.7^{a1}	37.6 ± 0.6^{a1}	37.8 ± 0.6^{a1}
	Incision	37.4 ± 0.4^{b1}	37.3 ± 0.8^{b1}	36.5 ± 1.4^{a1}	37.4 ± 0.3^{a1}
	Suture	37.0 ± 0.5^{b1}	37.0 ± 0.7^{b1}	36.8 ± 0.7^{b1}	36.9 ± 0.3^{b1}
	End	36.3 ± 0.5^{b1}	36.7 ± 0.6^{b1}	36.5 ± 0.8^{b1}	36.4 ± 0.5^{b1}

Table 2. Demographic data and time of duration of surgery, anesthesia, recovery and TAP + SSP block perform in each of the treatment groups submitted to total unilateral mastectomy.

Data	**Treatment group**			
	LG (*n* = 8)	**MtG (*n* = 8)**	**MxG (*n* = 8)**	**TG**
Age (years)	9 ± 2	8 ± 3.3	10.8 ± 3.5	10.9 ± 3.3
Body weight (Kg)	14.36 ± 5.67	13.99 ± 6.62	8.89 ± 7.51	13.9 ± 6.15
Breed	8 MBD	7 MBD; 1 Shih-tzu	7 MBD; 1 Poodle	7 MBD; 1 Poodle
Surgical time (min)	51.3 ± 7.4	51.3 ± 10.6	43.1 ± 14.6	53.8 ± 11.6
Anesthetized time (min)	76.3 ± 5.8	72.5 ± 12.5	65.6 ± 17.4	78.1 ± 11.0
TAP and SSP time (sec)	175 ± 55	-	-	271 ± 110
Extubation time (min)	4 ± 1.9	4.8 ± 2.7	5.6 ± 2.0	5 ± 2.2

Legend: MBD: Mixed breed dog.

Table 3. Propofol requirements for induction and maintenance, nociceptive and pain evaluation, analgesic rescues for the patients in each treatment group. Superficial serratus plane block with transversus abdomins plane block (LG, $n = 8$), preemptive meloxicam groups (MxG, $n = 8$), premedication methadone group (MtG, $n = 8$) and the association of these three techniques groups (TG, $n = 8$). Data was represented by mean ± standard deviation for normal distributed parameters, as median (range) for non-normal distributed parameters, and as proportions (%) for prevalence parameters. Statistical significance was considered when $p < 0.05$, and represented as (*) for difference between the treatment groups in the same line.

Parameters	Group			
	LG	MxG	MtG	TG
Propofol induction requirement (mg kg^{-1})	4.14 ± 1.12	5.03 ± 1.84	5.02 ± 0.80	4.68 ± 1.82
Propofol maintenance requirement (mg kg^{-1} min^{-1})	0.26 ± 0.05	0.28 ± 0.07	0.30 ± 0.07	0.33 ± 0.05
Animals that received fentanyl from the total in each group	5/8 (62.5%)	7/8 (87.5%)	6/8 (75%)	4/8 (50%)
Number of fentanyl administration in each groups from the total administration	7/39 (17.95%)	15/39 (38.46%)	10/39 (25.64%)	7/39 (17.95%)
Median number of fentanyl rescues per animal in each group	1 (0 – 2)	2 (0 – 4)	1 (0 – 4)	0.5 (0 – 3)
Total fentanyl dose per animal in each group (µg kg^{-1})	2.5 (0 – 5)	5 (0 – 10)	2.5 (0 – 10)	1.25 (0 – 7.5)
Time from the beginning of the surgery until the first rescue (min)	10 (10 – 20)	5 (5 – 30)	5 (5 – 30)	17.5 (5 – 35)
Animals with post-operative analgesic rescue from the total in each group	2/8 (25%)	0/8 (0%)	3/8 (37.5%)	1/8 (12.5%)
Number of post-operative analgesic rescues from the total rescues of the study	3/19 (15.8%)	0/19 (0%)	15/19 (78.9%)*	1/19 (5.3%)
Mean number of post-operative rescues per animal in each group	0 (0 – 2)	0 (0)	0 (0 – 6)	0 (0 – 1)
Total methadone dose per animal in each group (mg kg^{-1})	0 (0 – 0.6)	0 (0)	0 (0 – 1.8)	0 (0 – 0.3)
Time from extubation until eat (hours)	3 (1 – 20)	6 (1 – 20)	10 (2 – 16)	2.5 (1 – 24)

6. FINAL CONSIDERATIONS

This study is the first report of anatomical evaluation and landmarks definition of the superficial serratus plane block in dogs. With different volumes comparison. The SSP block is seem to be an easy to perform technique for veterinary anesthesiologists with minimal experience in ultrasound-guided blockades. Larger volumes of anesthetic solutions tend to cover a larger number of the lateral cutaneous nerves of the intercostal nerves. However, this difference is not statistically significant and a “small” volume of 0.3 mL kg^{-1} at SSP block, may be sufficient to cover the analgesia of the hemithorax from T1 to T9. Our clinical trials using SSP block associated with TAP block for total unilateral mastectomy using the volume determined at cadaveric study, showed encouraging results of postoperative analgesia up to 24 hours, without the use of concomitant analgesic medications such as opioids or NSAIDs. However, nociception stimulation may be a changeling with this techniques alones or combined with NSAID and opioid, as observed in this study, when the 20% of the baseline parameters just after induction (up to 15 minutes) was used as a trigger value. Other clinical uses of SSP block are encouraged to confirm all the analgesic possibilities of this novel technique.

7. REFERENCES

Allred C, Liu Y, Katrikh A et al. (2017) Cadaveric Study of Serratus Anterior Block. Annals of Emergency Medicine 70, 4S, S84.

Bailey CS, Kitchell RL, Haghighi SS et al. (1984) Cutaneous innervation of the thorax and abdomen of the dog. American Journal of Veterinary Research 45, 1689-1698.

Bajwa SJS, Anand S, Kaur G (2015) Anesthesia and cancer recurrences: The current knowledge and evidence. Journal of Cancer Research and Therapeutics 11, 3, 528 – 534.

Beswick A, Dewey C, Johnson R et al. (2016) Survey of Ontario veterinarians' knowledge and attitudes on pain in dogs and cats in 2012. Canadian Veterinary Journal 57, 1274-1280.

Bitti FS, Campagnol D, Rangel JPP et al. (2017) Effects of three methadone doses combined with acepromazine on sedation and some cardiopulmonary variables in dogs. Veterinary Anaesthesia and Analgesia 44, 237 – 245.

Blanco R, Parras T, McDonnell JG, Prats-Galino A (2013) Serratus plane block: a novel ultrasound-guided thoracic wall nerve block. Anaesthesia 68, 1107-1113.

Bolin RD, Harvey NR, Wilson SH (2015) Regional anesthesia for breast surgery: Techniques and Benefits. Current Anesthesiology Reports 5, 217 – 224.

Bruggink SM, Schroeder KM, Baker-Herman TL et al. (2012) Weight-based volume of injection influences cranial to caudal spread of local anesthetic solution in ultrasound-guided transversus abdominis plane blocks in canine cadavers. Veterinary Surgery 41, 455-457.

Cassi LC, Biffoli F, Francesconi D et al. (2017) Anesthesia and analgesia in breast surgery: the benefits of peripheral nerve block. European Review for Medical and Pharmacological Sciences 21, 1341-1345.

Castaneda-Herrera FE, Buritica-Gaviria EF, Echeverry-Bonilla DF (2017) Anatomical evaluation of the thoracolumbar nerves related to the transversus abdominis plane block technique in the dog. Anatomia Histologia Embryologia 46, 373 - 377.

Cata JP, Gottumukkala V, Sessler DI (2011) How regional analgesia might reduce postoperative cancer recurrence. European Journal of Pain Supplements 5, 345 – 355.

Chevallier DL, Slingsby L, Murrell JC (2018) Randomized clinical trial comparing clinically relevant sedation outcome measure in dogs after intramuscular administration of medetomidine in combination with midazolam or butorphanol for routine diagnostic imaging procedures. The Veterinary Journal 239, 30 – 34.

Corona D, Novello L (2018) Segmental thoracic epidural anaesthesia in a dog undergoing intercostal thoracotomy and lung lobectomy. Veterinary Record Case Reports 6, 1-6.

Credie LFG, Luna SP, Futema F et al. (2013) Perioperative evaluation of tumescent anaesthesia technique in bitches submitted to unilateral mastectomy. BMC Veterinary Reserarch 9, 178, 1-12.

Crociolli GC, Cassu RN, Barbero RC et al. (2015) Gabapentin as an adjuvant for postoperative pain management in dogs undergoing mastectomy. Journal of Veterinary Medical Science 77, 8, 1011-1015.

Downing R (2011) Pain management for veterinary palliative care and hospice patients. Veterinary Clinics of North America: Small Animal Practice 41, 3, 531 – 550.

Drozdzynska M, Monticello P, Neilson D et al. (2017) Ultrasound-guided subcostal oblique transversus abdominis plane block in canine cadavers. Veterinary Anaesthesia and Analgesia, 44, 183-186.

Evans HE, Lahunta A. *Miller's Anatomy of the Dog*. 4. ed. St. Louis: Saunders-Elsevier, 2013.

Fantoni DT (2011) Tratamento da dor na clínica de pequenos animais. 1ª ed, Rio de Janeiro, Elsevier.

Finucane BT. Complications of Regional Anesthesia. 2. Ed. Springer, 2007.

Freitag FAV, Bosak VL, do Carmo MPW et al. (2018) Continuous transverse abdominal plane block for analgesia in three dogs with abdominal pain. Veterinary Anaesthesia and Analgesia, 45, 581-583.

Getty, R. *Anatomia dos animais domésticos*. 5. ed. Rio de Janeiro: Guanabara Koogan, 1986.

Gorman NT, Dobson JM (1995) The skin and associated tissues. In: WHITE, R.A. S. Manual of Small Animal Oncology. Shurdington: British Small Animal, 187-200

Hellyer P, Rodan I, Brunt J et al. (2007) AAHA/AAFP pain management guidelines for dogs and cats. Journal of feline medicine and surgery 9, 466-480.

Hughes JML (2005) Anaesthesia for the geriatric dog and cat. Irish Veterinary Journal 61, 6, 380-387.

Khalil AE, Abdallah NM, Bashandy GM, Kaddah TAH (2017) Ultrasound-Guided Serratus Anterior Plane Block Versus Thoracic Epidural Analgesia for Thoracotomy Pain. Journal of Cardiothoracic and Vascular Anesthesia 31, 152-158.

Kim R (2018) Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence. Journal of Translational Medicine 16, 8, 1 – 13.

Kunhabdulla NP, Agarwal A, Gaur A et al. (2014) Serratus Anterior Plane Block for Multiple Rib Fractures. Pain Physician 17, E549-E557.

Lascelles BDX, McFarland JM, Swann H (2008) Guidelines for safe and effective use of NSAIDs in Dogs. Veterinary Therapeutics 6, 3, 237-251.

Lush J, Ijichi C (2018) A preliminary investigation into personality and pain in dogs. Journal of Veterinary Behavior 24, 62 – 68.

MacFarlane P (2018) Managing perioperative pain in dogs and cats. In Practice 40, 130 – 140.

Madabushi R, Tewari S, Gautam SKS et al. (2015) Serratus Anterior Plane Block: A new Analgesic Technique for Post-Thoracotomy Pain. Pain Physician 18, E421-E424.

Maria PP, Sobral RA, Daleck CR (1998) Casuística de cães portadores de neoplasias atendidos no Hospital Veterinário da Unesp / Jaboticabal durante o período de 01/01/95 a 01/05/97. In: CONGRESSO BRASILEIRO DE CIRÚRGIA E ANESTESIOLOGIA VETERINÁRIA, Anais Santa Maria: Colégio Brasileiro de Cirurgia e Anestesiologia Veterinária, 61.

Mathews KA (2000) Pain assessment and general approach to management. Veterinary Clinics of North America: Small Animal Practice 41, 531 – 550.

Mayes J, Davison E, Panahi P et al. (2016) An anatomical evaluation of the serratus plane block. Anaesthesia 71, 1064-1069.

McClure JH (1996) Ropivacaine. British Journal of Anaesthesia 76, 300-307.

Merlo DF, Rossi L, Pellegrino C et al. (2008) Cancer incidence in pet dogs: findings of the animal tumor registry of Genoa, Italy. Journal of Veterinary Internal Medicine 22, 4, 976–984.

Minto BW, Rodrigues LC, Stegall PVM et al. (2013) Assessment of postoperative pain after unilateral mastectomy using two different surgical techniques in dogs. Acta Veterinaria Scandinavica 55, 1 - 4

Moe L (2001) Population-based incidence of mammary tumours in some dog breeds. Journal of reproduction and Fertility – Supplement 57,439–443.

Morris J, Dobson J (2001) Mammary gland. In: MORRIS, J.; DOBSON, J. Small animal oncology. Iowa: Blackwell Science, 184- 189.

Morris JS, Bostock DE, Mcinnes EF et al. (2000) Histopathological survey of neoplasms in flat-coated retrievers, 1990 to 1998. The Veterinary Record 147, 291 – 295.

Morrison WB (1998) Cancer in Dogs and Cats: Medical and Surgical Management. Baltimore: Williams & Wilkins, 591-598.

Muir W, Berry J, Boothe DW et al. (2018) Opioid-Sparing Pain therapy in animals: Working Task Force.

Murrell J (2011) Clinical use of methadone in cats and dogs. Companion Animal 16, 56 – 61.

Nair AS, Sahoo RK, Ganapathy M, Mudunuri R (2015) Ultrasound guided blocks for surgeries/procedures involving chest wall (Pecs 1, 2 and serratus plane block). Anaesth, Pain & Intensive Care 19, 3, 348-351.

Nakagawa K, Miyagawa Y, Takemura N et al. (2007) Influence of preemptive analgesia with meloxicam before resection of the unilateral mammary gland on postoperative cardiovascular parameters in dogs. Journal of Veterinary Medical Science 69, 9, 939 – 944.

Portela DA, Romano M, Briganti A (2014) Retrospective clinical evaluation of ultrasound guided transverse abdominis plane block in dogs undergoing mastectomy. Veterinary Anesthesia and Analgesia 41, 319-324.

Portela DA, Verdier N, Otero PE (2018) Regional anesthetic techniques for the thoracic limb and thorax in small animals: A review of the literature and technique description. The Veterinary Journal 241, 8-19.

Reid J, Nolan AM, Hughes JML et al. (2007) Development of the short-form Glasgow Composite measure pain scale (CMPS-SF) and derivation of and analgesic Intervention score. Animal Welfare 16,97 – 104.

Retsky M, Rogers R, Demicheli R et al. (2012) NSAID analgesic ketorolac used perioperatively may suppress early breast cancer relapse: particular relevance to triple negative. Breast Cancer Research and Treatment 134, 881 – 888.

Sakonju I, Maeda K, Maekawa R et al. (2009) Relative nerve blocking proprieties of bupivacaine and ropivacaine in dogs undergoing brachial plexus block using a nerve stimulator. Journal of Veterinary Medical Science 71, 10, 1279 – 1284.

Sams L, Braun C, Allman D et al. (2008) A comparison of the effects of propofol and etomidate on the induction of anesthesia and on cardiopulmonary parameters in dog. Veterinary Anaesthesia and Analgesia 35, 488 – 494.

Sanches RC, Regonato E, Zilotto L et al. (2000) Doenças neoplásicas em cães: estudo retrospectivo de 535 casos. In: CONGRESSO BRASILEIRO DE CIRURGIA E ANESTESIOLOGIA VETERINÁRIA, Editora da Universidade Federal do Goiás 42.

Sano T, Nishimura R, Mochizuki M et al. (2003) Clinical usefulness of propofol as an anesthetic induction agent in dogs and cats. Journal of Veterinary Medical Science 65, 5, 641 – 643.

Schroeder CA, Snyder LBC, Tearney CC et al. (2011) Ultrasound-guided transversus abdominis plane block in the dog: an anatomical evaluation. Vet Anaesth Analg 38, 267–271.

Short CE, Bufalari A (1999) Propofol Anesthesia. Veterinary Clinics of North America: Small Animal Practice 29, 3, 747 – 778.

Sites BD, Gallagher JD, Cravero J et al. (2004) The learning curve associated with a simulated ultrasound-guided interventional task by inexperience anesthesia residents. Regional anesthesia and pain medicine 29, 544-548.

Sleeckx N, Rooster H, Kroeze EJBV et al. (2011) Canine mammary tumors, an Overview. Reproduction in Domestic Animals 46, 1112 – 1131.

Takimoto K, Nishijima K, Ono M (2016) Serratus plane block for persistent pain after partial mastectomy and axillary node dissection. Pain Physician 19, 481 – 486.

Teixeira LG, Pujol DM, Pazzim AF et al. (2018) Combination of Transversus abdomens plane block and Serratus plane block anesthesia in dogs submitted to mastectomy. Pesquisa Veterinária Brasileira 38, 2, 315-319.

Teixeira RCR, Monteiro ER, Campagnol D et al. (2013) Effects of tramadol alone, in combination with meloxicam or dipyrone, on postoperative pain and the analgesic requirement in dogs undergoing unilateral mastectomy with or without ovariohysterectomy. Veterinary Anaesthesia and Analgesia 40, 641-649.

Trapaidze N, Gomes I, Cvejic S et al. (2000) Opioid receptor endocytosis and activation of MAP kinase pathway. Molecular Brain Research 76, 220 – 228.

Uscagueti RAR, Feliciano MAR, Tiosso CF et al. (2017) Comparative Evaluation of Methadone Administration at Different Periods in Bitches Undergoing Mastectomy. Pakistan Veterinary Journal 37, 2, 345-349.

Uscagueti RAR, Tiosso C, Moro JV et al. (2016) Pre-emptive methadone or tramadol analgesia for mastectomy and ovariohysterectomy in bitches. Revista Colombiana de Ciencias Pecuarias 30, 39-47.

Varghese L, Johnson M, Barbeau M et al. (2016) The Serratus Anterior Plane (SAP) Block: An anatomical investigation of the Regional Spread of Anesthetic Using Ultrasound-guided Injection. The FASEB Journal 30, 1 supplement, 560.1-560.1.

Wang HJ, Chang SC, Lee WM et al. (2017) Comparison of Onsite Infiltration and Constant Rate Infusion for Postoperative analgesia in dogs with Mammary Tumors Undergoing bilateral radical mastectomy and ovariohysterectomy. Taiwan Veterinary Journal 43,3, 177 – 183.

Withrow SJ, Macewen EG (1996) Small Animal Clinical Oncology. 2. ed. Philadelphia: W. B. Saunders, 4-16.

Yi P, Pryzbylkowski P (2015) Opioid induced hyperalgesia. Pain Medicine 16, S32 – S36.

Zocca JA, Chen GH, Puttanniah VG et al. (2017) Ultrasound-Guided Serratus Plane Block for Treatment of Postmastectomy Pain Syndromes in Breast Cancer Patients: A Case Series. Pain Practice 17, 1, 141-146.